DIAGNOSIS OF CANINE HYPOTHYROIDISM

SOME CLINICAL AND LABORATORY METHODS

by

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ABSTRACT OF THESIS

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Title of Thesis Diagnosis of canine hypothyroidism some clinical and laboratory methods.

By detailed history taking and physical examination, 299 dogs, selected from the Clinic case-load, were placed in groups consisting of 47 cases of suspected hypothyroidism, (HS), 47 of other hormonal disease (OH), 99 of pyoderma (P), 57 of allergic dermatoses (A) and 49 of suspected ectoparasitism (EP). Groups P, A and EP were confirmed to be such by bacteriological and parasitological examinations and the presence of circumstances indicative of dermal allergy. For comparison, 68 normal dogs were available. There were statistically significant clinical differences between Groups HS and OH, the two most likely to afford difficulty in clinical differential diagnosis, in the incidence of alopecia, lethargy and above normal weight. Combinations of these were also much more frequent in Group HS. Other clinical features, especially of the skin, were sufficiently different in quality as well as numerically to separate all groups from Group HS.

Skin thickening is well known in hypothyroidism but the groin was the only one of 15 sites with significantly thicker skin in Groups HS and OH than the other groups. The difference was not due to breed influence which was, however, greater than that of hypothyroidism on the phase of hair growth. Twice as many HS dogs as others had subclinical anaemia but the incidence was low.

The occurrence of a breed incidence in hypothyroidism was confirmed. Dogs of larger breeds were not the more frequently affected. In Group HS, females were significantly more numerous than males and showed the first signs when younger. Proportionately more older animals were affected and neutered animals were at greater risk than entire animals.

Circulating cholesterol, protein bound iodine (PBI), serum glutamic oxalacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), serum alkaline phosphatase (SAP), cortisol, thyroxine (T4) and triiodothyronine (T3) were assayed. Cholesterol, T4 and T3 concentrations were unaffected by time of day and post-prandial interval but household scraps added to the diet raised cholesterol levels. Cholesterol levels were significantly higher in Group HS. Liver damage was indicated by high SAP values in untreated dogs of Group HS and OH dogs. Cortisol level response to adrenocorticotrophic hormone (ACTH) stimulation helped to identify cases of hyperadrenocorticalism as did skin biopsy histology. Sertoli cell tumours were confirmed histologically.

T4 and T3 levels differed significantly between some groups but did not partition Group HS from all others. Subnormal levels were present in some dogs of all groups. More precise partition of euthyroid from hypothyroid dogs, using in vitro methods only, would require additional tests such as thyroid stimulating hormone (TSH) assay or the response to TSH stimulation.

The relationship of breed, age and sex to 'base-line' levels of thyroid hormone and the possibility of (non-clinical) biochemical hypothyroidism predisposing to pyoderma require further investigation.

Use other side if necessary.
Use this side only.

This thesis has been composed by me and describes my own work except for those matters which are specifically referred to in the acknowledgements. It has not been submitted in any form for another degree or professional qualification.

S. H. Arslan

To the memory of my father

To my mother

and to

Tuna, Nasha and Sevgi

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INTRODUCTION

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Disorders of the canine skin and coat are frequently encountered in veterinary practice and because of their importance they have received a considerable amount of clinical and other forms of investigation. Hypothyroidism is one of the causes of these problems and it also gives rise to many other clinical manifestations, some of which are present in other diseases.

It seemed desirable to ascertain more precisely the frequency of the various clinical signs that predominate in hypothyroidism and to attempt to relate these signs not only to the clinical diagnosis supported by the results of non-specific laboratory diagnostic methods but if possible, to relate them to the results of specific diagnostic methods.

Since suspected hypothyroidism is encountered in veterinary clinics and hospitals as a practical problem requiring professional attention, the present investigation was based on dogs attending the Small Animal Clinic and the Department of Veterinary Medicine of the Royal (Dick) School of Veterinary Studies, University of Edinburgh, as patients. That is, the disease was not induced artificially but was studied as it occurred spontaneously. This approach has intrinsic problems such as are caused by the variation in the subjects due to their breed, age and sex, so that standard subjects with minimal variations and free of concurrent disorders are not available. The

flow of material for study depends not only on the natural occurrence of the disease but also on whether the owners will make their dogs available for repeated examinations or undertake continuous treatment.

Because standard cases of the artificially induced disease were not employed and because some clinical signs and laboratory findings in hypothyroidism overlap with those of other diseases, it was necessary to extend the investigation into a comparison of cases of suspected hypothyroidism with cases of other disease, as well as with normal dogs. The difficulties of clinical distinction are not great, for example from cases of external parasitism where a specific diagnosis is readily made. However, some other diseases are not readily distinguishable from hypothyroidism. These include some other endocrine diseases for which methods of definitive diagnosis are not readily available or have not yet been developed. Thus, at least one group of diseases for comparison with hypothyroidism has as many problems of diagnosis associated with it as has hypothyroidism itself, with the result that the approach to diagnosis and differential diagnosis required undertaking investigations on a rather broad front.

Early in the project it became evident that there was a great deal more overlapping of biochemical and other values in normal dogs and cases of suspected hypothyroidism and other diseases than many published accounts had implied. Accordingly, while the main part of the study had a clinical basis, consideration

was then given to whether a rather narrower biochemical definition of hypothyroidism could be associated with a group of clinical signs that could be used to improve the definition of clinically suspected hypothyroidism.

REVIEW OF THE LITERATURE

THE NORMAL THYROID GLAND

Anatomy of the Thyroid Gland

The following abbreviated description of the canine thyroid gland is from Hullinger (1979). The organ consists of paired lobes firmly attached laterally and somewhat ventrally to the outer surface of the proximal part of the trachea, between the fifth to eighth tracheal rings. The size varies with the breed, each lobe being approximately 5 cm long, 1.5 cm wide and 0.5 cm thick in medium sized breeds. In some dogs, there is a narrow connecting bridge of glandular parenchyma between the two lobes, passing across the tracheal surface ventrally. The cranial parathyroid glands lie near to or within the thyroid gland. The caudal parathyroids are embedded in the latter. The thyroid gland is highly vascularised from the cranial and caudal thyroid arteries, the former arising from the common carotid and the latter from the brachiocephalic artery. Within the gland, these vessels form anastomoses from which capillaries go to the follicles. From the gland, venous drainage is via the cranial and caudal thyroid veins which lead to the internal jugular vein. A similar drainage pattern is followed by the lymph vessels which pass to the cranial and caudal deep lymph nodes.

The thyroid nerve is formed by the cranial cervical

ganglion and the cranial laryngeal nerve. The nerve is believed to control blood flow to the gland but neither stimulation of the nerve nor denervation of the gland produces secretory or histological changes in the parenchyma.

Histology of the Thyroid Gland

Hullinger (1979) describes the fine structure of the gland as follows. Within the delicate capsule, there are septae and trabeculae bearing arteries, veins and lymphatic vessels. These divide the gland into lobules and bear the capillaries in a fine network. The main parenchymal units are follicles which are spheres, 50 - 900 mcm in diameter, filled with homogeneous colloid. The follicles are lined with simple epithelium which varies from low to high columnar, and which forms the thyroglobulin and thyroid hormones. Other nearby cells are "C" cells or parafollicular cells, which are larger than those of the follicle. The "C" cells secrete calcitonin.

Accessory Thyroid Tissue

Bloom (1971) noted that, in from 50 - 75% of dogs, accessory thyroid tissue occurs near the gland, in the region of the hyoid bone, within the thymus, along the cervical portion of the trachea, in the mediastinum, within the pericardium near the aortic arch, in peri-aortic

fat and subendocardially in the conus arteriosus. Many others, from Wolfler (1879) to Kallfelz (1977) have also reported abberant thyroid tissue in the dog.

Function of the Thyroid Gland

The following account is abbreviated mainly from Siegel (1977). Many other accounts have been presented. Basically, the thyroid gland produces and stores thyroid hormones, and secretes them in response to a feed-back mechanism which depends on the quality of the hormones in the circulation. Decreasing levels of circulating free thyroid hormones stimulate secretion of thyrotropin releasing factor (TRF) in the hypothalamus. The TRF is carried via the hypothalamo-adenohypophyseal portal system to the anterior pituitary gland where it stimulates the synthesis and release of thyrotropin or thyroid stimulating hormone (TSH). This passes via the circulation to the thyroid gland where it stimulates uptake of iodine, the synthesis of the hormones, the proteolysis of thyroglobulin and the release of hormone into the circulation.

The major function of the thyroid gland is to produce, store and release hormones that are involved in normal cellular metabolic activities.

Biosynthesis and Release of the Hormones

Together with iodide obtained from the breakdown of

thyroid hormone, inorganic iodine absorbed from the gut to the bloodstream produces serum iodide. The thyroid selectively extracts the iodide and excess amounts are excreted by the kidneys. (Excess thyroxine is excreted via the liver to the bowel, Gross & Pitt-Rivers, 1951-52). In the epithelial cells of the thyroid, the iodide is oxidised to iodine which immediately combines with tyrosine to form monoiodotyrosine (MIT) and diiodotyrosine (DIT). Two molecules of the latter combine to form one molecule of thyroxine (T4). This is secreted into the blood or combined with a peptide to form thyroglobulin for storage as colloid. A combination of MIT and DIT forms T3 which is similarly stored.

A protease liberates T3 and T4 from the stored thyroglobulin and they enter the blood stream to combine with plasmaproteins. T3 in the blood may also result from the deiodination of T4. In man, Evered (1976) states that 30 to 40% of the endogenous T3 is derived from extra-thyroidal conversion of T4 to T3.

Hormonal Transport

In the dog, serum T4 is bound to alpha globulin, albumin and to a third, electrophoretically distinct material "just ahead of the beta globulins" as Siegel puts it. Furth, Becker, Nunez and Reid (1968) have identified four T4-binding proteins in dog serum, namely

albumin, inter-alpha globulin and two beta globulins. In the dog, thyroxine binding protein (TBP) is in lower concentration than in other species, i.e. the binding capacity is not identical to that of man. TBP transports enough T4 throughout the body to allow a continuous supply of free hormones, on dissociation, to sustain cellular metabolism. The actual proportion of free T4 is tiny. In the dog it is 0.10 - 0.189% of total serum thyroxine (Sterling, 1968) but this is still a greater proportion of free T4 than is found in man.

Peripheral Hormone Metabolism

Deiodination of the thyroxine takes place at the cell surface, in the tissues, to form T3. The excess iodine returns to the blood. Both T4 and T3 have biological activity, that of the latter being much greater and more rapid. It is only the non-protein bound T4 or T3 that can diffuse into the tissues for metabolic purposes.

In dogs, T3 constitutes only a small fraction of the total plasma hormonal iodine (Rijnberk & van der Horst, 1969), as is also the case in man. The affinity of binding proteins for T3 is less than for T4 and this probably accounts for its greater potency and speed of action (Rijnberk, 1971).

Discovery of the Thyroid Hormones

Kendall discovered thyroxine in 1915, and it was

characterised and synthesised by Harington (1926) and Harington and Barger (1927).

Thyroglobulin was shown not to be normally present in the circulation (Lerman, 1940). The presence of an iodine-containing substance other than T4 was detected in animal plasma (Gross & Leblond, 1951a, b) and in human plasma (Gross and Pitt-Rivers, 1951). This was shown to be triiodothyronine (T3) by Gross and Pitt-Rivers (1952a, 1953a). They (Gross & Pitt-Rivers, 1952b, 1953b) found that, in rats, T3 was 3 to 4 or 5 times as active as T4 and they concluded that T3 is the peripheral thyroid hormone and that T4 was its precursor.

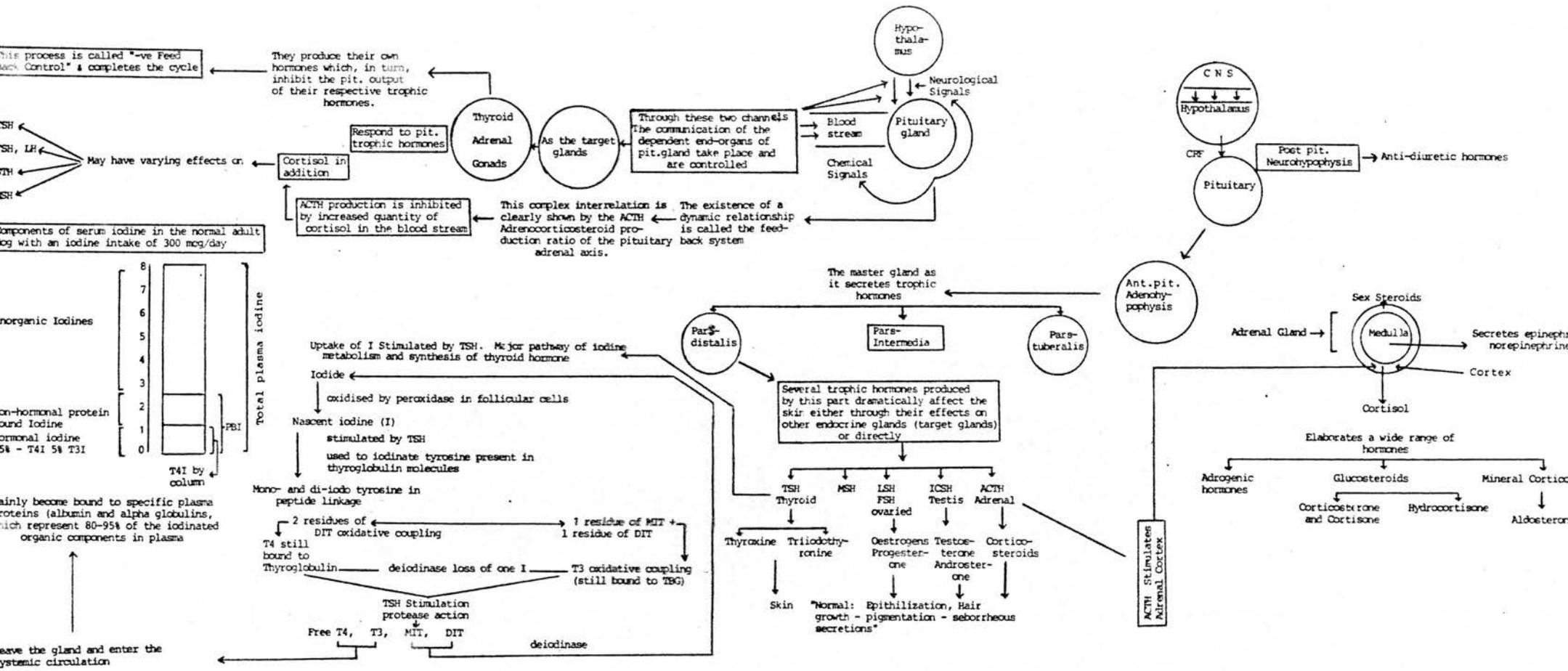
THE FEEDBACK SYSTEM OF HORMONE CONTROL

The diagram overleaf illustrates the relationship between the different parts of the endocrine system, with particular reference to thyroid function. The relevant references are Ettinger (1975), Bell, Emslie-Smith and Paterson, C.R. (1976), Muller & Kirk (1976) and Swenson (1977).

Abbreviations used

ACTH	Adrenocorticotropic hormone
STH	Somatotropic hormone
FSH	Follicle stimulating hormone
LH	Luteinizing hormone
ICSH	Interstitial cell stimulating hormone
MSH	Melanocyte stimulating hormone
TSH	Thyroid stimulating hormone
CRF	Corticotrophic releasing factor

THE FEED-BACK SYSTEM AND HORMONE CONTROL



DISEASES OF THE THYROID GLAND

Introduction

Many reviews and reports of diseases of the thyroid gland in the dog have been published dealing with aetiology and the structural and functional changes. As this thesis is concerned with spontaneous hypothyroidism, it is proposed to deal very briefly with the diseases of the gland generally and to refer to some of the salient publications only. Alterations of structure and size are associated with neoplasia (Clark & Meier, 1958; Meier & Clark, 1958; Groth, 1962b; Munson & Belshaw, 1966-67; Bush, 1969a, 1972a; Michaelson, 1969; Mason & Wilkinson, 1973; Siegel, 1977; Martin & Capen, 1979) and with simple goitre (Clark & Meier, 1958; Bush, 1969a, 1972a; Lievre, 1976). Congenital defects such as aplasia and hypoplasia occur (Munson & Belshaw, 1966-67; Jubb & Kennedy, 1970; Bush, 1969b, 1972a; Kallfelz, 1977; Siegel, 1977). Belshaw (1971) has referred to necrosis of the gland.

Inflammatory processes are recognised, including an auto-immune thyroiditis resembling Hashimoto's disease in man or lymphocytic thyroiditis (Beierwaltes & Nishiyama, 1968; Mawdesley-Thomas, 1968; Bush, 1969a, 1972a, 1979; Bustad & Fuller, 1970; Kaneko, 1970; Baker, 1971; Belshaw, 1971; Mason & Wilkinson, 1973; Schultz, 1974;

Capen, Belshaw & Martin, 1975; Lievre, 1976; Kallfelz, 1977; Siegel, 1977; Gosselin, Capen & Martin, 1978; Martin & Capen, 1979). Atrophy of the gland may follow inflammation of whatsoever cause and, in addition to the authors cited in connection with inflammation, this has been referred to by Freudiger (1962), Groth (1962b), Jubb & Kennedy (1963), Kral and Schwartzman (1964), Moser (1966), Thomsett (1966) and Siegel (1971). However, Capen, Belshaw and Martin (1975) and Bush (1979) consider that the loss of follicular epithelium may be neither a post-inflammatory nor autoimmune lesion but of unknown aetiology. This is idiopathic follicular collapse which, with lymphocytic thyroiditis is responsible for most clinical cases of primary hypothyroidism (Martin & Capen, 1979).

Functional changes also occur (Meier & Clark, 1958). Those associated with an insufficiency of circulating thyroid hormone cause hypothyroidism whereas an excess cause hyperthyroidism. The predominant disorder of canine thyroid function is hypothyroidism (Ekman, Orstadius & Thorell, 1968; Michaelson, 1969).

Aetiology of Hypothyroidism

Hypothyroidism in the dog may be primary or secondary, the latter being much less common.

Primary Hypothyroidism

The primary causes include thyroiditis (Jubb &

Kennedy, 1963; Munson & Belshaw, 1966-67; Bustad & Fuller, 1970; Kaneko, 1970; Schultz, 1974; Kallfelz, 1977; Siegel, 1977). Follicular atrophy is common and may be the commonest cause of primary hypothyroidism (Clark & Meier, 1958; Siegel & Belshaw, 1968; Bullock, 1970; Kaneko, 1970; Baker, 1971; Belshaw, 1971; Rijnberk, 1971, 1974; Bush, 1972a; Capen, Belshaw & Martin, 1975; Belshaw & Rijnberk, 1977). It is responsible for over 90% of the cases (Bush, 1977, 1979).

Congenital hypoplasia or aplasia is also a cause (Munson & Belshaw, 1966-67; Bush, 1969a, 1972a, 1979; Kallfelz, 1977; Siegel, 1977) and this may rarely give rise to canine cretinism. Other causes include neoplasia, the ingestion of goitrogens and iatrogenic procedures including surgical removal of the gland, its destruction by radioactive iodine and the administration of other substances (Munson & Belshaw, 1966-67; Bush, 1969a, 1972, 1979; Kallfelz, 1977; Siegel, 1977).

Iodine deficiency has been considered to be a cause of hypothyroidism (Michaelson, 1969; Kaneko, 1970; Mason & Wilkinson, 1973; Blakemore, 1974) but there is good agreement that this is rare in dogs (Munson & Belshaw, 1966-67; Bustad & Fuller, 1970; Bush, 1969a, 1972a; Siegel, 1971, 1977; Belshaw & Rijnberk, 1977; Kallfelz, 1977; Martin & Capen, 1979). It is unlikely to occur spontaneously as even the most severe degree of experimental iodine deprivation fails to cause it (Capen, Belshaw & Martin, 1975).

A number of other causes such as abnormalities of release of the thyroid hormones from the gland and errors in plasma binding or the transport mechanism have been mentioned by a number of workers but Munson & Belshaw (1966-67) have not observed them in dogs. Congenital defects in hormone synthesis may occur (Rijnberk, 1971) but are rare (Belshaw & Rijnberk, 1977). Siegel (1977) notes that various causes, identified in man, associated with specific enzyme deficiencies causing defective biosynthesis of hormones, have not been recognised in the dog. His experiments have suggested that although there may be hormone transport abnormalities in the dog, they are not the cause of a clinical abnormality. However he (Siegel, 1977) states that there are cases of clinical hypothyroidism in which the T4 levels are normal but which respond to thyroxine and he suggests these cases probably have an increase in unsaturated binding sites and a decrease in free circulating thyroxine. He also refers to the small number of cases of canine hypothyroidism which do not respond to the administration of oral sodium levothyroxine but which have an elevated serum thyroxine when the substance is given intramuscularly. He speculates as to whether these cases have a failure of intestinal absorption of thyroxine rather than that there is increased catabolism.

Secondary Hypothyroidism

Secondary hypothyroidism occurs in situations where the function of the thyroid gland is normal but in which other organs controlling its function are disordered. In adenohypophysis dysfunction (hypopituitarism and neoplasia) there may be impaired secretion of thyroid stimulating hormone (TSH). (Kral & Schwartzman, 1964; Moser, 1966; Munson & Belshaw, 1966-67; Thomsett, 1966; Bush, 1969a, 1972a, 1977, 1979; Bustad & Fuller, 1970; Kaneko, 1970; Siegel, 1971, 1977; Mason & Wilkinson, 1973; Capen, Belshaw & Martin, 1975; Kristensen, 1975b; Lievre, 1976; Belshaw & Rijnberk, 1977; Kallfelz, 1977; Martin & Capen, 1979) and most of these authors agree that less than 10% of cases are due to reduced TSH output. Less commonly, hypothalamic lesions prevent secretion of thyrotropin releasing hormone and also cause secondary hypothyroidism (Kristensen, 1975b; Kallfelz, 1977; Martin & Capen, 1979).

RELATIONSHIP OF HYPOTHYROIDISM TO HISTOLOGICAL CHANGES IN THE THYROID GLAND

As indicated in the section dealing with thyroid disease and the aetiology of hypothyroidism, a variety of lesions is incriminated. The following section deals with the histology of the main causes of hypothyroidism.

Clark and Meier (1958) and Meier and Clark (1958) made an extensive histopathological examination of canine thyroid glands and reported that only one-quarter of dogs, found to have histological lesions of the thyroid at post-mortem, had clinical signs in life. Furthermore, when clinical signs were present, they were independent, in some cases, of the type and extent of the lesion, i.e. the histology was not always an index of functional disturbance. Also, in many cases of goitrous, pre-cancerous and cancerous glands there had been no clinical signs in life. Bush (1979) stated that neoplasms are mainly euthyroid, sometimes hyperthyroid and rarely hypothyroid.

In laboratory beagles, histological thyroiditis occurs without causing clinical signs (Tucker, 1962; Bush, 1979). The lesion is focal (Musser & Graham, 1968), with an incidence of 0.4% (Mawdesley-Thomas, 1968) and is like Hashimoto's thyroiditis of man (Beierwaltes & Nishiyama, 1968). This is regarded as a form of autoimmune disease (Jubb & Kennedy, 1970) and is also referred to as lymphocytic thyroiditis and is only rarely found in thyroid biopsies from pet dogs with proved hypothyroidism (Belshaw, 1971; Belshaw & Rijnberk, 1977). It is an uncommon form of canine thyroiditis in which

the lesions are focal (nodular) or consist of diffuse, progressive infiltrations of lymphocytes, plasma cells and macrophages which replace the glandular tissue with lymphoid follicles often having well-developed germinal centres (Jubb & Kennedy, 1970; Baker, 1971; Belshaw & Rijnberk, 1977; Martin & Capen, 1979). Hypothyroidism only occurs when 75% or more of the follicles are lost (Belshaw & Rijnberk, 1977).

The other, much commoner, lesion is that in which the follicular structure is lost in varying degree. This can be severe. The origin is unknown and it is referred to as idiopathic or acquired primary atrophy. The follicular epithelium is extensively lost to be replaced by adipose connective tissue. Only a few viable follicles remain with small nests of parafollicular cells and accumulations of lymphocytes (Jubb & Kennedy, 1970; Baker, 1971; Capen, Belshaw & Martin, 1975; Belshaw & Rijnberk, 1977; Bush, 1979). This is the form of thyroiditis which is usually associated with clinical signs of hypothyroidism (Capen, Belshaw & Martin, 1975; Belshaw & Rijnberk, 1977).

In secondary hypothyroidism due to thyroid stimulating hormone deficiency, the follicles are distended with accumulated colloid and the epithelium is flattened (Capen, Belshaw & Martin, 1975).

Use is made of this knowledge in the examination of thyroid gland biopsy samples taken for histological examination. Routine biopsy for diagnostic purposes is

useful and reliable in cases of primary acquired atrophy where the glandular atrophy is gross (Baker, 1971; Capen, Belshaw & Martin, 1975; Belshaw & Rijnberk, 1977). Such examination effectively distinguishes hypothyroid and normal dogs and discriminates between primary and secondary hypothyroidism (Bush, 1979). Siegel (1977), however, refers to varying degrees of thyroiditis being found in routine biopsy specimens from dogs that showed no signs of thyroid disease. Reference has already been made to Clark and Meier (1958) and Meier and Clark (1958) who reported the imprecise relationship to the clinical picture or its absence, in dogs in which the glandular lesions were fully examined microscopically after death. Evered (1976) states that in man, neither needle (drill) biopsy nor fine needle (aspiration) biopsy obtains representative samples of thyroid for histology. He considers satisfactory samples can only be obtained by open surgery. His view is that there is little indication for routine, or other, thyroid biopsy.

The main deficiency of the reports cited is a lack of numerical data regarding the frequency of occurrence, on thyroid biopsy examination, of idiopathic (acquired, primary) atrophy of the gland in euthyroid and apparently euthyroid dogs and conversely, the frequency with which the lesion is detected at biopsy in clinically affected dogs. At this stage, examination of biopsy speciments can only be regarded as one of a battery of tests. If positive

results are obtained in a clinical case this would be helpful, but the absence of specific lesions in such a case or their presence in a euthyroid dog is not likely to be helpful in diagnosis. This is an important subject but does not fall within the scope of the present thesis.

CLINICAL SIGNS OF HYPOTHYROIDISM

Introduction

The clinical signs of acquired primary hypothyroidism in the dog are of gradual or insidious onset as has been noted by numerous authors including Goyings (1961-62), Goyings, Reineke and Schirmer (1962), Moser (1966) and Orstadius (1971). Cases are usually presented to the veterinarian 3 to 9 months after the onset of the first signs (Rijnberk, 1971, 1974; Belshaw & Rijnberk, 1977). The different signs vary in their time of onset and intensity depending on the age of the patient, duration of thyroid hormone deprivation and whether the lack of hormone is partial or complete (Bush, 1969a; Rijnberk, 1971, 1974; Kallfelz, 1977). Although the disorder is often regarded as mainly affecting the integument to the extent that Maahs (1958-59) regarded the main sign as diffuse alopecia, it affects the whole body (Munson & Belshaw, 1966-67).

Physical and Mental Lethargy

The first indication of hypothyroidism is a change in the dog's interest in exercise and it gradually becomes physically lethargic or sluggish (Holmes, 1933; Coffin & Munson, 1953; Maahs, 1958-59; Meier & Clark, 1958; Kaneko, 1960, 1970; Goyings, 1961-62; Goyings

et al., 1962; Greve & Gaafar, 1964b; Mallo, 1966; Moser, 1966; Schwartzman, 1966; Theran & Thornton, 1966; Thomsett, 1966; Michaelson, Quinlan, Casarett & Mason, 1967; Ekman, Orstadius & Thorell, 1968; Reid, 1968; Bush, 1969a, 1972a, 1977; Michaelson, 1969; Bustad & Fuller, 1970; Jubb & Kennedy, 1970; Belshaw, 1971; DiScala, Lippe & Segal, 1971; Orstadius, 1971; Rijnberk, 1971, 1974; Siegel, 1971, 1977; Mason & Wilkinson, 1973; Blakemore, 1974; Chester, Hightower, Kyzar & Wright, 1974; Schultz, 1974; Capen, Belshaw & Martin, 1975; Schalm, 1975; Lievre, 1976; Muller & Kirk, 1976; Martin & Capen, 1979). Belshaw and Rijnberk (1977) noted that in each of 13 cases of acquired primary hypothyroidism, there was a history of lethargy. This physical slowing-down is also manifested, as many of these authors have noted, in sleepiness, reluctance to walk and the rapid onset of fatigue when required to take exercise. Although this is the usual picture, Capen et al. (1975) consider that some may be vigorously active.

The sluggishness is not only of the body; there is development of apathy, listlessness and depression including a delay in the animal's response to a favourite food, announcement of a walk or a loud noise (Meier & Clark, 1958; Freudiger, 1960, 1962; Hoffer, 1962; Kral & Schwartzman, 1964; Ekman et al., 1968; Muller & Kirk, 1969; Jubb & Kennedy, 1970; Kyzar, Chester & Hightower, 1972; Rijnberk, 1971, 1974; Schalm, 1975;

Belshaw & Rijnberk, 1977; Bush, 1977; Crispin & Barnett, 1978).

Theran and Thornton (1966) noted a case which had a history of 8 months of lethargy prior to its presentation for examination. Generally, the affected dogs are quietly stupid and good-natured but they may become cantankerous (Maahs, 1958-59; Freudiger, 1960, 1962; Kral & Schwartzman, 1964; Bush, 1969a). They are seldom excited or nervous when being examined (Belshaw, 1971) and although Rijnberk (1971, 1974) refers to one of his six cases behaving in this way, the other five were quiet and good-natured.

Belshaw (1971) regards the physical lethargy and dull mental attitude as being amongst the most frequent and prominent signs and so characteristic of hypothyroidism in the dog that they, rather than alopecia or obesity, should be considered the cardinal signs that would alert the veterinarian to the diagnosis. However, some cases remain bright and alert although showing other prominent signs compatible with hypothyroidism.

The Skin

Generally, veterinary attention is sought because of changes in the dog's skin and coat as these are probably the most obvious signs and often the cause of the owner's concern (Bush, 1969a; Baker, 1971;

Kallfelz, 1977). Not all hypothyroid cases have skin lesions (Muller & Kirk, 1969), up to one-third of hypothyroid dogs not having grossly visible skin changes on first examination (Belshaw 1971). Blakemore (1974) even considers that integumental changes are not particularly common in canine hypothyroidism although hypothyroidism is probably blamed for many skin problems.

The skin changes take longer than the other signs to develop (Goyings, 1961-62), requiring over 2 to 6 months (Goyings et al., 1962). Although the skin has been described as smooth (Coffin & Munson, 1953; Goyings, 1961-62), especially in alopecic areas (Martin & Capen, 1979), and thin (Coffin & Munson, 1953; Meier & Clark, 1958; Goyings, 1961-62; Jubb & Kennedy, 1970), more often this is not the case and these authors and others comment on the other, more frequent changes such as that it is harsh, rough, wrinkled or superficially ridged (Holmes, 1933; Meier & Clark, 1958; Schalm, 1965, 1975; Reid, 1968; Bush, 1969a; Muller & Kirk, 1969, 1976; Bustad & Fuller, 1970; Mason & Wilkinson, 1973; Thomsett, 1975; Kallfelz, 1977).

It is widely accepted that an important clinical change in the skin is that it becomes thickened (Borgman & Reineke, 1950; Freudiger, 1960; Goyings, 1961-62; Goyings et al., 1962; Hoffer, 1962; Moser, 1966; Munson & Belshaw, 1966-67; Thomsett, 1966; Bush, 1969a, 1972a, 1977; Michaelson, 1969;

Schalm, 1975). This was observed in 11 of 13 cases by Belshaw and Rijnberk (1977). Sometimes the thickening is regarded as a puffiness, swelling or sponginess (Meier & Clark, 1958; Ekman et al., 1968; Bush, 1969a; Baker, 1971; Orstadius, 1971; Rijnberk, 1971). Belshaw and Rijnberk (1977) describe it as puffiness in 9 out of their 13 cases. Variously, these authors refer to the affected areas as being the head and face, especially above the eyes, the throat, the neck, the back and, more generally, the trunk. In the giant breeds the extremities are affected (Kirk, 1979).

The thickening which is not of the epidermis (Munson & Belshaw, 1966-67; Martin & Capen, 1979), but of the dermis and subcutis, which is indurated and doughy (Reid, 1968), may fall into folds on the forehead and about the throat, the former giving the patient what Rijnberk (1971) and Capen et al. (1975) have described as a "tragic appearance" which is contributed to by blepharoptosis (Rijnberk, 1971; Belshaw and Rijnberk, 1977). As Bush (1969a, 1977) has indicated, it is in the chronic or advanced cases that such marked changes are present. The altered skin loses its elasticity (Rijnberk, 1971; Kristensen, 1975b). Similar skin changes have been described in dogs that have been thyroidectomised (for example, Greve & Gaafar, 1964b).

Much consideration has been given as to whether the skin swelling is myxoedematous (as in the hypothyroid

adult human) and, on grounds of physical examination, some have asserted that there is no true or typical myxoedema (Bloom, 1959; Hoffer, 1962; Mallo, 1966; Munson & Belshaw, 1966-67; Ekman et al., 1968; Orstadius, 1971). Goyings (1961-62) has expressed opinions both that it may or may not exist. Nonetheless the opinion of Smith & Jones (1957) and Hoffer (1962) is that the possibility should be considered, and Kral and Schwartzman (1964) consider that it does occur rarely. Martin and Capen (1979) state unequivocally that myxoedema of the dermis may develop and produce a characteristic clinical appearance in long-standing or severe cases. In these cases the skin feels thick and doughy but does not show the pitting characteristic of other types of oedema. In experimentally induced hypothyroidism, DiScala et al., (1971) report the occurrence of myxoedema. This matter will be considered again when histological changes are reviewed.

Scaliness, as an aspect of hyperkeratosis, is commonly described (Meier & Clark, 1958; Goyings, 1961-62; Goyings et al., 1962; Hoffer, 1962; Mallo, 1966; Munson & Belshaw, 1966-67; Reid, 1968; Muller & Kirk, 1969; 1976; Belshaw, 1971; Orstadius, 1971; Chester et al., 1974; Thomsett, 1975; Bush, 1977; Crispin & Barnett, 1978). Although Theran and Thornton (1966) consider less than half of the cases have hyperkeratosis, Martin and Capen (1979) regard

it as a consistent finding. The hyperkeratinisation may be most marked in the axillae and inguinal regions (Moser, 1966) or other friction sites (Mallo, 1966) including the edges of the ears which become thickened (Rijnberk, 1971). The hyperkeratosis may become severe and occur in circular scaling patches suggestive of seborrhoea and also by accumulating in the hair follicles distend them to form comedones (Conroy, 1979; Martin & Capen, 1979). Sometimes lichenified areas appear as irregular plaques or crusted debris on the skin surface (Goyings, 1961-62; Schalm, 1975) adding to the scurfiness. Bush (1969a) cites Groth (1962a) that the excessive scurf is probably caused by lack of vitamin A resulting from liver dysfunction.

Associated with the scaliness, the skin is dry (Holmes, 1933; Maahs, 1958-59; Meier & Clark, 1958; Freudiger, 1962; Hoffer, 1962; Mallo, 1966; Reid, 1968; Bush, 1969b; Muller & Kirk, 1969, 1976; Bustad & Fuller, 1970; Kaneko, 1970; Orstadius, 1971; Mason & Wilkinson, 1973; Thomsett, 1975; Lievre, 1976). In experimentally induced hypothyroidism, half of 18 dogs had dry skin (Greve & Gaafar, 1964a).

Thus, although dryness of the skin is well reported, other changes may occur to cause an excessive oiliness (Chester et al., 1974; Schalm, 1975). This is an indication of the secondary seborrhoea that occurs in some cases and which may cause a foul odour (Goyings, 1961-62; Goyings et al., 1962; Muller & Kirk, 1969, 1976).

The action of the sebaceous glands is controlled by the sex and other hormones, probably of distant origin, acting locally on the hair follicles or taking part in epidermal cell division (Ebling, 1965; Amoroso & Ebling, 1966). Anderson (1974) considers the factors predisposing to seborrhoea to be endocrine disturbances, faulty diet and unfavourable environment but remarks that the primary causal factors have not been ascertained. The affected skin, he notes, affords a good medium for the growth of micro-organisms. Austin (1974) refers to seborrhoea sicca and seborrhoea oleosa in the dog as having a familial tendency in cocker and springer spaniels. The more severe form, sebopsoriasis, tends to occur in poodles and cocker spaniels. Rojko, Hoover and Martin (1978) recorded seborrhoea in 5 of 28 cases of hypothyroidism which they distinguished from the other or "classical" cases. They, like Conroy (1979) did not associate pruritus with the seborrhoeic cases. Ihrke (1979) states that hypothyroid-induced seborrhoea, or at least thyroid hormone-responsive seborrhoea, occurs quite commonly in the dog but not necessarily in association with the typical (classical) picture of the obese, lethargic heat-seeker. He considers that Dobermans, Irish setters or Afghan hounds show an increased frequency of hypothyroid-related seborrhoea.

Generally, pruritus is not present in hypothyroidism and when it does occur (Goyings et al., 1962) as, for example, in the inguinal area or ears (Mallo, 1966),

it is due to causes other than hypothyroidism. Pruritus is usually only evident when seborrhoea or secondary infection is present. Secondary infection has been reported by Goyings et al.(1962), Moser (1966) and Thomsett (1975). Bush (1969a) and Ihrke (1979) note that seborrhoea and secondary infection are fairly frequent complications, especially of the skin folds. The associated lesions are either very slow to heal or do not heal (Ojemann, 1940; Kirk, 1947; Goldberg & Chaikoff, 1952; Coffin & Munson, 1953; Goyings et al., 1962; Bush, 1969a; Thomsett, 1975).

The skin is cool or even cold to the touch (Moser, 1966; Goyings, 1961-62; Ekman et al., 1968; Muller & Kirk, 1969; Orstadius, 1971; Crispin & Barnett, 1978), especially after the hair is lost (Mason & Wilkinson, 1973).

In advanced cases, increased pigmentation of the skin occurs, especially of the areas that have become denuded of hair or are subject to friction (Coffin & Munson, 1953; Goyings, 1961-62; Goyings et al., 1962; Hoffer, 1962; Kral & Schwartzmann, 1964; Walton, 1965; Mallo, 1966; Moser, 1966; Theran & Thornton, 1966; Ekman et al., 1968; Reid, 1968; Bush, 1969a, 1972a, 1977; Muller & Kirk, 1969, 1976; Orstadius, 1971; Mason & Wilkinson, 1973; Chester et al., 1974; Thomsett, 1975; Lievre, 1976; Kallfelz, 1977; Martin & Capen, 1979). The areas of hyperpigmentation

are especially the neck and dorso-lateral aspects of the thoracic and lumbar regions, as well as the axillae and inguinal region (Mallo, 1966). In 3 of 6 cases the inner aspect of the pinna was also pigmented (Rijnberk, 1971), and Martin and Capen (1979) note its occurrence in the denuded dorsal aspect of the nose and distal parts of the tail. According to Theran and Thornton (1966) somewhat less than half of hypothyroid cases show hyperpigmentation of the skin but Belshaw and Rijnberk (1977) recorded it in 10 of their 13 patients. Bornfors (1958), cited by Kral & Schwartzman (1964), Walton (1965) and Schwartzman (1966) describe the change in some cases as being acanthosis nigricans. Kirk (1979) summarising informations on patients with acanthosis nigricans concludes that the great majority are not hypothyroid. Hyperpigmentation also occurs in experimentally induced cases (DiScala et al., 1971; Kyzar et al., 1972).

Other dermatological or integumentary features reported include the following. Otitis, described as ceruminous (Goyings et al., 1962) or as chronic and bilateral (Munson & Belshaw, 1966-67; Muller & Kirk, 1969, 1976), is commonly associated with hypothyroidism. Less commonly, there may be impaction of the anal glands (Goyings, 1961-62; Goyings et al., 1962). Dogs with eczematous conditions often have a coexisting hypofunctioning thyroid (Tiecken, 1956, cited by Kral & Schwartzman, 1964). The induced

disease neither exacerbates nor causes remission of demodicosis (Greve & Gaafar, 1964b). Thomsett (1966) observed severe wear of the antero-dorsal aspect of the claws in advanced cases.

The Coat

All of the authors already cited who have reported skin changes have also described or discussed alterations in the coat and it is not proposed to repeat all of their names here. The coat changes are of gradual onset and occur in both male and female dogs whether entire or castrated or spayed. The hair first loses its lustre and in mild cases there may be simply a dry, thin coat. With time, or increased severity of the hypothyroidism, the hair becomes brittle and breaks easily, leaving a short coat at the points of wear. It is easily epilated. Progressively there is increased hair loss described by many as excessive or unseasonal shedding. Ekman et al. (1968), however, consider that abnormally severe shedding is only occasionally seen and Rijnberk (1971) and Belshaw and Rijnberk (1977) record that in some short-haired dogs such as the boxer there may be a very thick coat due to retarded hair growth and defective shedding. Blakemore's (1974) experience is that the delayed rate of hair growth (which is widely recorded) may result in decreased exchange of hair and less shedding than expected and that shedding

may actually increase when thyroid replacement therapy is instituted.

The remaining hair is said to be fine and fuzzy (Coffin & Munson, 1953; Meier & Clark, 1958) but most describe it as coarse and scanty, e.g. Belshaw and Rijnberk (1977) who so describe 12 of their 13 cases.

Although the coat is thinned generally in some cases, complete hairlessness is rare. The alopecia of advanced cases starts as patches of baldness which coalesce and may affect any part of the body but much more usually the affected sites are those most exposed to pressure or rubbing as these remove the hair from the follicle. Joshua (1958) noted that the owners often ascribed it to "collar rub". The main areas are the neck, chest, back, abdomen, flanks, hips, lateral and caudal aspects of thighs, ear flaps and tail. It is rare for the head and the lower parts of the limbs to be affected. The alopecia tends to be bilaterally symmetrical.

Walton (1965) regards the alopecia as a disturbance of the hair cycle, i.e. as a form of hormonal dermatosis, which may be due to initiation of anagen in the resting follicle. However, Schwartzman (1966) believes it may result from the hormonal imbalance causing the hair follicles to go into the resting or telogenic state. Martin and Capen (1979) state that in hypothyroidism there are increased

numbers of hair follicles in the telogen phase.

Bilaterally symmetrical alopecia occurs in about one-half of hypothyroid dogs (Capen et al., 1975; Kristensen, 1975b; Muller & Kirk, 1976) and was reported in 7 of their 13 cases by Belshaw and Rijnberk (1977). However, Meier and Clark (1958) observed it in only 10% of their 38 canine cases. Theran and Thornton (1966) also consider the incidence to be low and Belshaw (1971) noted that, at the first examination of his patients, one-third of them had no grossly visible changes of the hair coat.

The non-pruritic bilaterally symmetrical alopecia described is not, of course, pathognomic of hypothyroidism. The authors already cited describe it as being similar to that seen in other endocrine disorders such as Cushing's syndrome (first reported as a cause of bilaterally symmetrical alopecia by Coffin and Munson, 1953) hyperoestrinism, Sertoli cell tumour, hypopituitarism and hypoandrogenism. The true incidence of hormonal alopecia is not known but Gregor (1965) working in the same clinic as the present writer, recorded an overall incidence of 0.5% in the dog and Thomsett (1975) recorded 0.85%. Schwartzman (1966) recorded hormonal alopecia as occurring in 5% of all his patients.

Increase in Body Weight

Many authors report that canine hypothyroid patients

have an increase in weight which may come on suddenly and be sufficiently great in some cases for the patients to be described as obese (Coffin & Munson, 1953; Clark & Meier, 1958; Maahs, 1958-59; Bryan, 1960; Freudiger, 1960, 1962; Kaneko, 1960; Goyings, 1961-62; Hoffer, 1962; Lombardi et al., 1962; Reed & Femino, 1963; Kral & Schwartzman 1964; Walton, 1965; Moser, 1966; Schwartzman 1966; Theran & Thornton, 1966; Mallo, 1966; Thomsett, 1966; Michaelson et al., 1967; Munson & Belshaw, 1966-67; Ekman et al., 1968; Bush, 1969a, 1972a, 1977; Muller & Kirk, 1969; Jubb & Kennedy, 1970; Bustad & Fuller, 1970; Orstadius, 1971; Seigel, 1971, 1977; Mason & Wilkinson, 1973; Blakemore, 1974; Schalm, 1975; Capen et al, 1975; Lievre, 1976; Muller & Kirk, 1976; Kallfelz, 1977; Crispin & Barnett, 1978; Martin & Capen, 1979). These authors lay varying emphasis on the weight gain or obesity and are agreed that obesity is not an essential feature and that hypothyroidism may be associated with non-obese or even thin animals. Meier and Clark (1958) recorded obesity in 9 of 38 cases and commented, as did Goyings (1961-62) with 16 out of 27 cases, that it was more frequently present than alopecia. Belshaw and Rijnberk (1977) found increased body weight in 8 of their 13 cases. Michaelson (1969) regarded it as an important point in diagnosis and considered it to reflect a reduction in the metabolic rate.

Some authors observed it in dogs with reduced

or, at least, not increased appetites (Bryan, 1960; Hoffer, 1962; Theran & Thornton, 1966; Rijnberk, 1971; Martin & Capen, 1979). Others acknowledged it to be due to overeating or hypothalamic lesions. Belshaw (1971) associated it with overeating and Buser (1974) referred to excess of food rich in fat causing lipaemia and cholesterolaemia and inducing simple obesity. Anderson (1973) discussed canine obesity in detail and noted that factors other than hypothyroidism required consideration, as it was probably the commonest nutritional canine abnormality in the United Kingdom. Edney (1972) reported a survey of 1134 dogs in which it was found that 34% (range 25 - 44%) of all dogs were obese and in which 68% of 81 spayed bitches were obese. It would thus appear that the incidence of obesity is higher in spayed bitches than in the total population.

Anderson (1973) also referred to the general impression that castrated male dogs were more prone to obesity than other dogs but the figure given of 4 in 10 male castrates in the survey reported by Edney (1972) does not appear to support this view. However, the number involved is too small to draw meaningful conclusions.

Dogs subjected to thyroidectomy also showed weight gain (DiScala et al., 1971; Kyzer et al., 1972; Chester et al., 1974).

Thermophilia (Heat Seeking)

Thermophilia, that is, a desire on the part of the hypothyroid dogs to seek warmth or to be intolerant

of cold, is widely reported (Munson & Belshaw 1966-67; Theran & Thornton, 1966; Bush, 1969a; 1972a, 1977; Bustad & Fuller, 1970; Belshaw, 1971; Siegel, 1971, 1977; Rijnberk, 1971, 1974; Chester et al., 1974; Schultz, 1974; Capen et al., 1975; Kallfelz, 1977; Martin & Capen, 1979). Munson and Belshaw (1966-67) and Bush (1969a) remark that this is a difficult matter to assess. Rijnberk (1971, 1974) notes that these dogs can tolerate high temperatures without panting. Siegel (1971) puts it as approximately second in relative frequency as a clinical sign. Sensation of cold occurred in 12 of 13 cases (Belshaw & Rijnberk, 1977), i.e. it was second only to lethargy as a sign in their list. Thus heat-seeking is an important consideration in the provisional diagnosis.

Body Temperature

The thermophilia is associated with the lowered basal metabolic rate referred to by Dott (1923), Binswanger (1936), Borgman and Reineke (1950), Hoffer (1962), Kral and Schwartzmann (1964), Bush (1969a) Rijnberk (1971, 1974), Blakemore (1974) and Kallfelz (1977). This, in turn, is reflected in a body temperature which is lower than normal (Goyings, 1961-62; Goyings et al., 1962; Hoffer, 1962; Ekman et al., 1968; Bush, 1972a, 1977; Muller & Kirk, 1976; Kallfelz, 1977). In 5 of 6 cases (Rijnberk, 1971,

1974) the body temperature was subnormal, with a range of 37.8 - 38.3°C. Nine of 13 cases had low body temperature (Belshaw & Rijnberk, 1977). Ten normal and 5 hypothyroid Alsatians had mean rectal temperatures of 38.6 $\pm$ 0.09 and 37.8 $\pm$ 0.18°C (Crispin & Barnett, 1978), i.e. a significant difference ($P < 0.01 > 0.001$).

The Pulse

The pulse rate is slower than normal. The normal rate is 139 $\pm$ 25 per minute (Hamlin, Olsen, Smith & Boggs, 1967). Joshua (1958) regarded a sluggish, soft pulse as an important feature. Bradycardia is reported by Freudiger (1960, 1962), Goyings (1961-62), Hoffer (1962), Kral and Schwartzman (1964), Moser (1966), Thomsett (1966), Ekman et al. (1968), Bush (1969a, 1972a, 1977), Siegel (1971) and Muller and Kirk (1976). Belshaw (1971) describes the heart rate as being moderately slow at 60 - 80 per minute and contrasts this with the mild tachycardia manifested by most dogs undergoing examination. Rijnberk (1971, 1974) found the pulse to be weak and slow in 5 of his 6 cases, at 79 - 96 per minute. In 5 of their 13 cases there was a low pulse rate (Belshaw & Rijnberk, 1977). In 4 cases the rates were 96 - 100, 56 - 60, 87 - 95, and 82 - 86 per minute (Crispin & Barnett, 1978). Martin and Capen (1979) note that it may be difficult to demonstrate conclusively that the heart rate has slowed if it

was not determined previously, as the change may be subtle.

Rijnberk (1971, 1974) notes there is a decreased cardiac output and that the apex beat is hard to detect. In 9 of 13 cases reported by Belshaw and Rijnberk (1977) the apex beat was weak. In contrast, Bryan (1960) reported a pounding heart and related this to the anaemia associated with hypothyroidism.

Reproduction

A relationship of hypothyroidism to abnormalities of reproductive function and behaviour, in advanced cases especially, is frequently referred to, e.g. Goyings et al. (1962) state that 6 of 50 hypothyroid cases "had breeding trouble". Joshua (1958) thought there was a degree of impotence in male dogs. Behaviourly, decreased or lost libido in male dogs is commonly reported (Freudiger, 1960; Goyings, 1961-62; Goyings et al, 1962; Walton, 1965; Munson & Belshaw, 1966-67; Bush, 1969a, 1972a, 1977; Michaelson, 1969; Siegel, 1971, 1977; Belshaw, 1971; Blakemore, 1974; Muller & Kirk, 1976; Kallfelz, 1977). Capen et al. (1975) considers libido not to be noticeably affected but that spermatogenesis is markedly decreased, the latter also having been noted by Belshaw (1971). Testicular atrophy has been reported by Mallo (1966), Rijnberk (1971, 1974) and Bush (1977). Small testes were present in 4 of 7 hypothyroid male dogs (Belshaw & Rijnberk, 1977) and

in all 4 male Alsatians reported by Crispin and Barnett (1978).

Hypofunction of the gonads often follows hypothyroidism and is also referred to by Ekman et al. (1968), Kaneko (1970) and Orstadius (1971). The infertility in females may be marked by failure to conceive or a poor conception rate (Blakemore, 1974) or by early abortion (Capen et al., 1975). Otherwise, the female may show signs of lengthened, irregular or abnormal oestrus cycles, decreased duration or intensity of oestrus, or cessation of oestrus (Joshua, 1958; Freudiger, 1960; Goyings et al., 1962; Moser, 1966; Munson & Belshaw, 1966-67; Bush, 1972a, 1977; Rijnberk, 1971, 1974; Siegel, 1971, 1977; Blakemore, 1974; Capen et al., 1975; Muller & Kirk, 1976). A normal oestrus cycle may be followed by pseudocyesis (Hoffer, 1962). Occasionally there is prolonged bleeding of up to 2 or 3 weeks in the cycle although the other physical signs of oestrus are much reduced (Belshaw, 1971; Capen et al., 1975). Sometimes the pro-oestral bleeding is replaced by a white discharge for a few days (Rijnberk, 1971, 1974). Belshaw and Rijnberk (1977) reported absence of oestrus in 5 hypothyroid bitches.

It is of interest that in experimentally hypothyroidectomised dogs, Kallfelz (1977) considered the reproductive function to be normal.

Musculo-Skeletal System

Goyings et al. (1962) described signs suggestive of arthritis. Arthralgia and myalgia and muscular and joint stiffness occur occasionally (Munson & Belshaw, 1966-67; Michaelson, 1969; Kallfelz, 1977). Bush (1969a) cites Groth (1962a) that there is weakness of muscle due to muscle degeneration and states that this can produce herniae in severe cases. Martin and Capen (1979) state that there is impaired joint function with clinical evidence of pain, and joint effusion also may result from severe or prolonged hypothyroidism.

Reed and Femino (1963), in confirmed cases of canine hypothyroidism, record radiographically the presence of calcification and herniation between the intervertebral discs, T7 to L13. In twenty cases of hypothyroidism induced by radio-thyroidectomy, 3 cases had signs of arthralgia or myalgia with reluctance to walk, which was especially prominent when the environmental temperature was low (Chester et al., 1974). Sims, Redding and Nachreiner (1977) reported depressed thyroid function in 2 tetraplegic dogs. Greene, Knecht and Roesel (1979) found a significant correlation when the age, breed and sex of dogs with intervertebral disc disease and hypothyroidism were compared, using information from 14 United States and Canadian Veterinary Schools. Furthermore, in investigating 100 dogs clinically affected with intervertebral disc disease, they found that 54% were hypothyroid and 20% were

suspicious, in terms of the results of combined T3-T4 tests. They carefully point out that this does not establish a causal relationship, but that the data strongly suggest a correlation in the physical characteristics of dogs affected with the two conditions.

Digestive Tract

Alteration in digestive tract function occurs occasionally and usually takes the form of constipation, which might be intermittent (Freudiger, 1960; Munson & Belshaw, 1966-67; Reid, 1968; Bustad & Fuller, 1970; Belshaw, 1971; Siegel, 1971; Bush, 1972a, 1977; Muller & Kirk, 1976; Kallfelz, 1977; Martin & Capen, 1979). Rijnberk (1971, 1974) states that constipation is a common sign of hypothyroidism in man but he did not observe it in his six canine cases and Capen et al. (1975) consider constipation to be uncommon, although the faeces are usually firm and somewhat dry. Belshaw and Rijnberk (1977) recorded constipation in 2 of 17 cases. Rijnberk (1971, 1974) had one case in which the owner reported diarrhoea as the main sign. Others (Munson & Belshaw, 1966-67; Belshaw, 1971; Muller & Kirk, 1976; Bush, 1977; Siegel, 1977) indicate that occasionally mild diarrhoea is present.

The Voice

Altered vocalisation has been reported in hypothyroid

dogs. Meier and Clark (1958) observed a lack of barking and Rijnberk (1974) and Belshaw and Rijnberk (1977) refer to hoarseness as occasionally occurring, the latter indicating that two of their 13 cases were so affected. Walton et al. (1965) have referred to the husky voice in hypothyroid human patients.

Other Clinical Signs

Other signs, unimportant from a diagnostic viewpoint, which have been reported are occasional rhinorrhoea without another specific cause being assigned (Munson & Belshaw, 1966-67), stomatitis (Reid, 1968), decreased output of urine (Rijnberk, 1971); and hernia (Bush, 1972a, 1977). The occurrence of blepharoptosis contributing to a tragic facial appearance (Rijnberk, 1971), has already been noted.

The report (Crispin & Barnett, 1978) of the first association, in the dog, of hypothyroidism with secondary lipoproteinaemia and arcus lipoides cornea is of interest. It is manifested physically by a clear zone at the corneal periphery and the perilimbal zone of the sclera. It takes the form of circular bands which may or may not be complete.

SUBCLINICAL HYPOTHYROIDISM

There are probably as many subclinical cases of hypothyroidism as there are of those of the overt variety (Munson & Belshaw, 1966-67). In human medicine the term is used to indicate a condition characterised by some of the non-specific signs of hypothyroidism plus a low metabolic rate and is often caused by non-thyroidal disease (Kurland, Hamolsky & Freedberg, 1955; Zimmer & Collins, 1967). Bush (1969a) suggests that this could explain some of the cases in which clinical signs of hypothyroidism are occasionally seen in the dog but in which there is no demonstrable lesion in the thyroid gland. However, Jubb and Kennedy (1970) are among those who have noted that some cases of this kind respond to thyroid therapy. Bloom (1971) called cases showing physical signs of hypothyroidism, but in which there was no authentic evidence that thyroid lesions were causing the signs, 'questionable hypothyroidism' and remarked that these cases frequently responded to thyroid treatment.

In veterinary work generally, the description 'subclinical' is confined to disease conditions which are not appreciated as being present by the unaided senses of a trained and experienced clinician. The authors cited above, with the exception of Munson & Belshaw (1966-67), appear to be referring to some clinically

observed condition and not a subclinical one, although it may not of course be hypothyroidism. Accordingly, the present author would prefer to call the condition 'pseudohypothyroidism' if it is clinically manifested but is not actually the result of thyroid disease and no other specific diagnosis has been made. The suggestion of Bloom (1971) that the observed disorder may be called 'questionable hypothyroidism' is also a useful one. To 'pseudohypothyroidism' should be added appropriate descriptions such as 'clinically mild' or 'severe' 'chronic' or 'acute' and 'thyroxin responsive' or 'thyroid stimulating hormone responsive'.

Evered (1976) used the term 'subclinical hypothyroidism' in man in the way in which the present author understands it in the dog, that is to describe a condition without clinical signs but in which tests revealed the presence of a thyroid gland functioning at a level below that regarded as normal. However, Hoffenberg (1977) objected to the continued use of the term 'subclinical hypothyroidism' as he found it hard to define and feared that its acceptance would give rise to misunderstanding and unnecessary therapy. Nonetheless, Fowler (1977) noting that some other experts in the field shared Hoffenberg's view, considered that unnecessary thyroxine therapy based on a misunderstanding could scarcely be an adequate reason for rejecting the validity of a concept.

Generally, in veterinary medicine, reference has not been made to subclinical hypothyroidism although many workers have found apparently normal dogs with T3 or T4 levels below the normal range. These results are referred to in the appropriate section of the review.

INCIDENCE OF HYPOTHYROIDISM

Introduction

Less information than one would expect is available in the form of statistical analysis on the breed, age and sex incidence of acquired, primary hypothyroidism, especially when, as Kral and Schwartzman (1964) and Belshaw (1971) state, it is one of the more commonly occurring endocrine diseases of the dog and is relatively frequent. Kallfelz (1977) states that it is the commonest of the thyroid disorders in canine practice.

Breed Incidence

Its occurrence in different breeds has been recorded. In 50 cases, Goyings, Reineke and Schirmer (1962) reported it in 11 cocker spaniels (22%), in 7 dachshunds and beagles together (14%) and then in a further 17 breeds or mongrels. Of these, 11 were of the larger breeds. They did not correlate their observations with the dog population of the area. Borgman and Reineke (1949) considered English bulldog puppies to be hypothyroid individuals. Chow Chows are predisposed to hypothyroidism (Holmes, 1933), suggesting an inherited tendency (Joshua, 1958). Rijnberk (1971) in 6 cases, recorded it in one dachshund;

the other patients were of the larger breeds. Bush (1972a, 1977, 1979) and Belshaw and Rijnberk (1977) found the incidence to be higher in the larger breeds, e.g. retrievers, setters and spaniels. In 16 cases, Lievre (1976) recorded it in 5 poodles and 2 Irish setters. Muller and Kirk (1976) state that there is a breed predilection in English bulldogs, golden retrievers, Irish setters, spaniels and basenjis.Greene, Knecht and Roesel (1979) refer to the dachshund, Doberman pinscher, golden retriever, Irish setter and cocker spaniel as having a higher occurrence of hypothyroidism than other breeds, based on statistics of cases of all canine disease entering 14 United States and Canadian Veterinary Schools. It appears to be uncommon in miniature or toy breeds (Bush, 1979).

Age Incidence

Although according to Coffin and Munson (1953) it is seen in all ages of dogs, it is most frequently found in middle aged (Maahs, 1958-59) or older animals (Meier & Clark, 1958), the average being 5.7 years with a range of 1.5 to 11 years (Goyings et al., 1962). It is most common over 3 years of age (Walton, 1965) and tends to occur between 6 and 9 years (Schwartzman, 1966), that is, in adults (Jubb & Kennedy, 1970). Other ranges given are 2 to 5 years (Rijnberk, 1971; Belshaw & Rijnberk, 1977 and 3 to 5 years (Bush, 1972a). Lievre (1976) reported a mean age of 4.5 years. Generally it is the middle aged and older dogs that are the most frequently affected (Capen, Belshaw & Martin, 1975; Bush, 1977). Significantly more dogs with hypothyroidism were in the 4 to 10 year age range ($P < 0.01$) than in the general

hospital population previously referred to (Greeneet al., 1979).

There is an interrelationship between the occurrence of hypothyroidism, breed and age referred to by Muller and Kirk (1976) who, having indicated the breed predilections stated above, say it may occur in older dogs of any breed, but that in the giant breeds, e.g. Great Dane, St. Bernard and Newfoundland, it can occur at an earlier age, namely 2 to 5 years. Such breeds are often affected before middle age (Bush, 1979).

The age incidence of the clinical disease in dogs is rather different from that in other domesticated mammals for in them most of the clinical features are not observed in the adults except that the adult females may have prolonged gestation, dystocia or be of low fertility generally. The effects are mainly seen in their offspring, which have a high rate of neonatal mortality and varying degrees of goitre, alopecia and myxoedema (Jubb & Kennedy, 1963).

However, congenital hypothyroidism does also occur in the dog, in which it resembles the cretinism of human offspring (Bryan, 1960) rather than the congenital goitre observed in the offspring of farm animal species affected by iodine deficiency. Bush (1969b; 1972a; 1977) describes these canine cretins as being seldom encountered and as having a stunted physical development being dwarfed with a broad skull and short thick legs. Rijnberk (1971) described it in a pointer bitch which was 4 years old when he examined her. The patient's growth was retarded, the

legs were disproportionately short and there was a long standing bilaterally symmetrical alopecia.

Sex Incidence

The gender of the patients has also been reported. Coffin and Munson (1953) and Walton (1965) recorded it in male, female and neutered dogs of both sexes. Meier and Clark (1958) found no evidence that thyroid disease resulted from spaying or castration inducing hormonal imbalance in early life. Maahs (1958-59) considered it to be more common in spayed bitches, and Jovanovic et al. (1959) considered that castration of the male rat reduced thyroid activity, but Bush (1969a) stated that these reports had not been confirmed and that the available evidence suggests that the incidence is unaffected by removal of the gonads. Both sexes are equally affected (Goyings et al., 1962; Bush, 1969a; 1972a). Of 6 cases, 4 were female and 2 male (Rijnberk, 1971). The 16 cases reported by Lievre (1976) consisted of 7 males and 9 females. On the basis previously noted, Greeneet al. (1979) found no difference between entire male and female dogs, but that significantly more ($P < 0.01$) spayed females had hypothyroidism than other dogs.

SKIN THICKNESS

Introduction

Many authors have stated that the skin is affected in hypothyroidism. Some of the descriptions have been subjective but others were the result of histological examinations. This is referred to elsewhere. Some of the histological examinations have included measurements of skin thickness. However, few measurements appear to have been made on the intact living animal.

Skin Thickness in the Living Dog

Hauck (1949) noted the lack of information about skin thickness in different breeds. In 98 adult dogs of different breeds with healthy skins, Hauck established the general state (softness, stiffness), fold height (looseness, elasticity) and the thickness. By thickness, Hauck meant the double thickness of the fold of skin when taken up by the fingers. He measured the fold thickness in seven places: the crown, scruff, withers, croup, shoulder, side of chest and knee fold (belly). The skin varies in thickness at different sites. Generally, it is soft but where the hair is coarse and hard, the skin also is coarser, for example the wire-haired fox terrier has very coarse thick skin, which is stiff and inelastic, on its back. The West

Highland White terrier also belongs to this group whereas, e.g. greyhounds are in the group of mainly fine-skinned dogs, with fewer differences in thickness between sites.

The pattern of variation in skin thickness over the body is the same in all pedigree dogs (Brunsch, 1956).

Dall (1958) stated that the skin becomes thicker with age, but Baker (1966) considered that, because of the decrease in subcutaneous fat, the skin is thinner.

THE HAIR

In the dog, the patterns of length, density, growth rate and loss of hair are affected by breed or genetic factors and the area of the body (Klatt, 1948; Brunsch, 1956; Kirk, 1971; Kristensen, 1975a; Thomsett, 1975; Burns, 1978; and see reviews by Blackburn, 1965; Walton, 1965) as well as by the animal's age (Baker, 1966). The effect of endocrine activity has been reviewed by Blackburn (1965), Ebling (1965), Walton (1965), Amoroso and Ebling (1966), Thomsett (1966) and Kirk (1971). Walton (1965) has also reviewed the effect of season, climate and other environmental factors.

The normal mode of hair replacement varies in different species, one mode consisting of periodic activity with neighbouring follicles in the same phase (Durward & Rudall, 1949) as is the case in the dog (Comben, 1951). The dog has a definite moulting period, generally in early autumn, and there is often another in the spring (Burns, 1943). The thinner coat in summer indicates a reduced functional capacity of the follicles at this time (Brunsch, 1956). Photoperiod may be more important than temperature, the coat being shed as the photoperiod decreases (Ebling, 1965) and when dogs are kept in household conditions there may be little if any seasonal variation in hair loss (Thomsett, 1966). In male beagles kept outside during the day and housed at night, Al-Bagdadi, Titkemeyer and Lovell (1977)

found the greater hair shedding was in spring and autumn, the two telogen peaks occurring at the time of seasonal temperature change. Anagen reached its maximum in summer and winter, following a curve which was almost the mirror image of the telogen one.

The hair is also affected by diseases either locally affecting the skin, as is common knowledge, by diet or nutritional deficiencies (Burns, 1943; Coffin & Munson, 1953; Thomsett, 1966) or by systemic diseases such as those of endocrine origin. Endocrine dysfunctions affecting the hair include hypothyroidism, to which considerable reference has already been made, and Sertoli cell tumour, canine Cushing's syndrome and other pituitary and gonadal disorders (see e.g. Coffin & Munson, 1953; Thomsett, 1966; Baker, 1974b). In these conditions the hair follicles become atrophic and inactive, resulting in the cessation of the normal cycle of shedding and regrowth. The hairs remain in the follicles until they are removed by mechanical abrasion, leading to bilaterally symmetrical alopecia. The inactive or resting stage is known as the telogen stage.

Ebling (1965) states that the effect of the steroids, the hormones of the gonads or adrenal cortex, tends to prolong the telogen stage and thyroid hormone may shorten it. Ebling (1965) describes and defines the processes as follows. Anagen is the active growth phase in which hair is produced by mitosis of cells in the matrix around the dermal papilla. The middle region of the hair bulb

starts to become constricted. Above this, the hair root is expanded and keratinised to form a club. At the transitional or catagen stage, the connective tissue sheath of the follicle thickens and becomes corrugated just below the newly formed club. This cord of cells pushes the club hair up the hair canal. The distal portion of the hair follicle left in the canal below the club shortens to become the secondary germ. This is now the telogen or resting stage. When the next period of activity (anagen) starts, often weeks or months later, the secondary germ elongates, grows down to enclose the dermal pillar and gives rise to the new hair bulb from which a new hair grows upward to emerge beside the old club which is then lost. Ebling continues, severe illness or systemic stress such as pregnancy or parturition may shorten the anagen stage and cause many body hairs to enter telogen prematurely, but in a synchronised fashion. The altered hormonal balance at parturition may also be a stimulus to end anagen, causing the moult in lactating bitches which has been referred to by, e.g. Thomsett (1966), Baker (1974a) and Kristensen (1975a).

Little reliability can be placed on hair loss for diagnosing disease. To attempt to differentiate the endocrine diseases on the basis of the pattern of hair loss is difficult because these changes are only indications that the normal follicular cyclical growth process has become synchronous and all follicles within an area are in telogen (Thomsett, 1966, 1975).

Kristensen (1975b) reported on 5 cases of T4-responsive alopecia in dogs that were not obviously hypothyrotic except one. The hair follicles, examined by skin biopsy, were all in telogen in 2 cases (including the dog believed to be a hypothyroid case), mostly in telogen in a third case, half in telogen and half in anagen in the fourth and mostly in anagen in the fifth.

PROTEIN BOUND IODINE

Protein Bound Iodine Assay in Assessing Canine Thyroid Function

It has been well known to medical science for many years that hormonal iodine is bound to proteins in the blood stream and this has been made use of in tests which measure plasma protein bound iodine (PBI), so that the state of thyroid function may be assessed (e.g. Trevorrow, 1939). The level of PBI is decreased in hypothyroidism. PBI has also been assayed in veterinary medicine and by 1940, Riggs and Man reported that it had been applied on various species of domestic animals.

Danowski, Man and Winkler (1946), Mayer (1947) and Glock (1949) concluded that dogs were less dependent than man on thyroid hormone because the former had lower PBI values which, in their opinion, indicated less thyroxine, although the amounts of serum thyroxine binding globulin (TBG) were similar. The number of TBG sites unoccupied would thus be greater in the dog than in man.

Gross and Pitt-Rivers (1952a) considered that the PBI level would be elevated above that of thyroxine alone because T3 precipitation also occurred as well as that of other iodinated proteins of which thyroglobulin would be the commonest.

A number of workers (Meier & Clark, 1958; Wilson, Dickson & Frost, 1961; Hoffer, 1962; Mallo, 1966; Quinlan & Michaelson, 1967; Michaelson, 1969) considered that assay of PBI was both reliable and significant in measuring canine thyroid function.

Kaneko, Tyler, Wind and Cornelius (1959), Dimopoullos (1963), Kral and Schwartzman (1964) and Ekman, Orstadius and Thorell (1968) noting that PBI concentrations were relatively low in the dog, stated that this limited the value of PBI assay for measuring the degree of experimental hypothyroidism.

Mallo and Harris (1967) and Muller and Kirk (1969) regarded all the iodine which is protein bound to be thyroid hormonal iodine, as did also Michaelson (1969) who assumed that T4 did not exist in significant free amounts in the plasma. Although most of the organically bound iodine in plasma, in man and some domestic animals, is considered to be hormonal, this had not yet been proven to be so in the dog (Bustad & Fuller, 1970). In fact, it was becoming obvious that canine PBI did not contain thyroid hormone alone as its source of iodine and Munson and Belshaw (1966-67) considered that a wider range of tests should be carried out on hypothyroid patients to ensure diagnostic accuracy. Considerable error occurred due to the high level of inorganic iodine in the serum of most dogs (Siegel & Belshaw, 1968).

Accordingly, before the final analysis of PBI, inorganic iodides should be completely removed, otherwise chemical determination of PBI would be of little value. Even minute amounts of extraneous iodine could contaminate the sample and give erroneous results.

Bullock (1970) reported that in the dog only 40 - 60% of PBI is from thyroxine, compared with 80 - 90% in man. Refetoff, Robin and Fang (1970) agreed that the non-hormonal iodides present add to the difficulty of interpretation of the test.

Bush (1970a) drew attention to the fact that T3 is biologically more potent than T4, i.e. less T3 is needed to supply the normal physiological effect. As well as altering the T3 : T4 ratio (compared with man), this may explain the lower PBI level in canine serum compared with human serum (Farran & Bush, 1971).

According to Mason and Wilkinson (1973) about 90% of canine PBI is derived from thyroxine.

In man, the diagnostic efficiency of PBI values seemed to be satisfactory, if contaminated specimens were excluded from assay (Clark, 1975; Hoffenberg, 1975; Bold & Browning, 1975). Nevertheless, these workers found that 20% of hypothyroid human patients had normal PBI levels. It was then realised that although the measurements were accurate for human subjects, their significance was an important matter that had not been sufficiently considered.

While the situation in human medicine was as described, in veterinary medicine it had become increasingly clear that PBI assay was inadequate for diagnostic purposes because it was non-specific for serum T4 concentrations due to the possibility of contamination by many other forms of iodine.

Hightower and Miller (1969) considered that although PBI levels were often low, they still frequently remained within the normal range in dogs that were apparently affected with hypothyroidism. They concluded from this that PBI assay was not an acceptable test because of its unreliability as an indicator of thyroid status. More and more, veterinary workers were appreciating that the chemical determination of serum PBI was of little value in diagnosis, especially because of the presence of non-hormonal iodine as contamination (Kaneko, 1963; Kral & Schwartzman, 1964; Schalm, 1965; Munson & Belshaw, 1966-67; Bustad & Fuller, 1970; Kallfelz, 1973; Rijnberk, 1974; Capen, Belshaw & Martin, 1975; Lorenz & Cornelius, 1976; Bush, 1977). Their view was that the hormonal iodine was not distinguished from the non-hormonal iodine in PBI. Capen et al. (1975) considered that the concentration of PBI was related not to the thyroid function but to iodine intake. As Lorenz and Cornelius (1976) stated, the test had been largely replaced as a measure of serum thyroxine concentrations by other tests which were more accurate and specific. Siegel

(1977) pointed out that the reliability of the test had been based entirely on the assumption that it predominantly measured hormonal iodine bound to protein and this had been shown to be wrong.

Factors Affecting PBI Concentrations

The plasma concentration of PBI may be affected by factors intrinsic to the dog, e.g. its breed, age, sex and state of health, or by extrinsic factors, i.e. substances which when administered to the dog affect the level. This is, of course, apart from the sample being contaminated by environmental iodine during collection, storage or analysis.

Effect of breed. Mallo and Harris (1967) found no effect of breeds on PBI in 25 normal dogs, nor did Bush (1970a) in his investigations. Nunez, Becker, Furth, Belshaw and Scott (1970) reported that the Basenji had a lower serum protein-bound radio-iodine value than European breeds of dogs (Shetland collie, cocker spaniel and beagle). The differences were significant, the mean value in the Basenjis being 2.2 mcg/100 ml and in European breeds being 3.3 mcg/100 ml of $PB^{127}I$. All of their dogs were maintained on the same diet, therefore the lower $PB^{127}I$ concentrations found in the Basenjis was not likely to be due to a difference in dietary iodine intake. They

suggest that the lower value found in the Basenjis may reflect a difference in intra-thyroidal metabolism of iodine or in the binding of thyroid hormones by plasma proteins and/or their rate of degradation. Rijnberk (1971), in 30 adult dogs, found no influence on PBI due to breed but accepted that the number was too small for any definite conclusion to be reached.

Effect of age. Mallo and Harris (1967) noted no effect of age on PBI values in 27 euthyroid dogs. Quinlan and Michaelson (1967) found no differences due to age in 37 normal male and female dogs. Nunez et al. (1970) also found no significant differences. Rijnberk (1971) considered that the values were higher in young dogs than in adults.

Effect of sex. Komarova, Sokolova and Tendler (1965), cited by Bush (1970a), reported that PBI is lower in normal male dogs than in females but neither Mallo and Harris (1967) nor Rijnberk (1971) observed this.

The PBI values are raised in pregnancy in a number of species, e.g. the cow (Barker, 1954; Kiesel & Burns, 1960), women (Tepperman, 1962; Clark, 1975) but not in the mare (Irvine, 1967). In pregnancy, there is an increase in the thyroxine binding proteins which take up more of the free form of the hormone from plasma.

In man, oestrogen is reported to increase (Bullock, 1970; Davies, 1972) and androgen to decrease (Bullock, 1970) the PBI values by increasing or decreasing the plasma concentration of thyroxine binding globulin. Bullock referred to unpublished data of Belshaw (1968)

who suggested that in the bitch PBI concentration may increase during oestrus and pregnancy, but that conclusive data had yet to be obtained. Rijnberk (1971) reported that, in the dog, the thyroxine binding capacity is greatly increased in pregnancy and during oestrogen treatment, giving elevated PBI levels. Lorenz and Cornelius (1976) also remarked that oestrogen may elevate PBI levels by increasing the amount of TBG.

Effect of time of year. Kelsey, Gullock & Clausen (1960) found the mean PBI values in October to be almost double those recorded in March. The two groups of dogs studied were not the same and no explanation for the difference is given. The possibility is that this may reflect an increased metabolic rate in the dogs studied in October as compared with those studied in spring, because of colder weather in October, but in the absence of fuller information, this is speculation.

Effect of disease. Apart from thyroid dysfunction, the PBI level may be affected by diseases such as nephrosis and hepatic cirrhosis (Blackburn and Power, 1955). Cases with hypoproteinaemia should be excluded from PBI measurement (Murphy, Pattee & Gold, 1966) because the level of binding proteins is reduced, thus lowering the PBI (Davies, 1972).

Effect of drugs and other substances. In human medicine, PBI assays are frequently invalidated due to iodine ingested in drugs or introduced into the body as the radio-opaque dyes used in radiography, (Murphy, Pattee & Gold, 1966). Pharmacological doses of iodine cause PBI to remain elevated for three or four weeks after administration has ceased (Siegel & Belshaw, 1968). Some of the extraneous iodine introduced into the body for therapeutic, prophylactic or diagnostic purposes, can become protein-bound and circulate for weeks to years. Such sources include the use of tincture of iodine as a skin disinfectant and of dinitrophenol (DNP) as an anthelmintic in dogs. Another anthelmintic, phenothiazine, inhibits the uptake of iodine by the thyroid gland because of its high iodine content. This is in keeping with the knowledge that a high intake of iodine itself may inhibit the organic binding of iodine (Jubb & Kennedy, 1970). Other factors affecting the PBI level include oestrogens, sulphonamides, long-term high dosage with ACTH and cortisone. Virtually all drugs containing organic iodine invalidate the PBI test in dogs (Baker, 1971) and man (Acland, 1971). Many of these compounds, but not DNP, can be separated from thyroid hormone by ion exchange column chromatography. This is the great advantage, Baker stated, of the T4 column test.

The presence of mercurial diuretics causes falsely

low PBI values (Elking & Karat, 1968; Singh, Hebert & Gault, 1972; Siegel, 1977). Salicylate also lowers PBI because it competes with T4 and T3 for binding sites on TBG (Davies, 1972). Many workers have commented on the problem of interpreting PBI results in dogs that have had iodine-containing radiographic dye administered to them. For example, Siegel (1977) noted that the effect lasted for at least a week but that the effect of the oil-based dyes may persist for several months.

Daily supplements of vitamin A induce a slight but definite increase in serum PBI levels in man (Danowski, Wirth, Black, Barton & Bastiani, 1955) and in domestic animals (Kaneko, 1970).

Great care must thus be taken in ensuring that the dog has not been treated in any of the ways mentioned before PBI measurements are made. Care is also needed to avoid extraneous contamination by iodine when taking the sample and by ensuring that the container used is free of all iodine contamination and that the estimation is undertaken at a laboratory that is aware of the problems of contamination (Theran & Thornton, 1966; Mallo & Harris, 1967; Thomson & Michaelson, 1967; Siegel & Belshaw, 1968; Hightower & Miller, 1969; Michaelson, 1969; Muller & Kirk, 1969; Rijnberk, 1971).

Kaneko (1970) considered that the degree of contamination could be assessed by measuring the total

serum iodine and if this were over 25 mcg/100 ml, the PBI result should be considered equivocal. When total serum iodine values are high, this produces falsely high PBI values (Siegel, 1971; Ekman, 1976) and special precautions should be taken to remove iodine contamination from canine serum before PBI levels are estimated (Mason & Wilkinson, 1973; Lorenz & Cornelius, 1976; Kallfelz, 1977; Siegel, 1977), for example by an ion exchange resin (Bustad & Fuller, 1970; Rijnberk, 1974). This is not the same technique as that of measuring thyroxine by column using an ion exchange resin.

Effect of dietary iodine. Bush (1970b) reviewed the factors causing elevation and errors in the results of PBI determinations. These include diet and he (Bush, 1972b) considered that the differences between his results and those of others could be ascribed to differences in the iodine content of the different diets. Since many pet foods are fortified with excessive amounts of inorganic iodine, causing errors in interpreting the results of thyroid function tests, a diet low in iodine should be fed for 7 - 10 days before sampling (Baker, 1971). To obtain a clearer base line, Farran and Bush (1971) fed a proprietary dog food from which the iodine-containing dye, erythrosine, had been omitted. Rijnberk (1971), in a particular series of dogs, found that the iodine consumption varied only slightly and PBI values also showed little

variation, although the mean PBI values increased with the amount of iodine fed.

Effect of thyroxine. In dogs, thyroxine administration raised the PBI concentration and the free thyroxine level, but it did not change the total T4 (Hollander, Thompson, Barrett & Berlin, 1967). It takes one or two weeks before the effects on PBI of desiccated thyroid or thyroxine given as medication disappear (Kaneko, 1970). When hypothyroid dogs are treated with adequate but not excessive doses of thyroxine or desiccated thyroid, the serum PBI concentration usually goes to levels above the normal range (Belshaw, 1971).

Protein Bound Iodine Concentrations in the Dog

Normal dogs. Plasma PBI values in normal dogs have been reported in the literature variously as single figures, averages, ranges and means ± standard deviations.

In view of the various criticisms expressed about the significance of the values and the fact that the method has been largely superseded by more accurate and meaningful ones, the results reported are simply given chronologically (in mcg/100 ml plasma) as follows: nil - 2.4 (Riggs & Man, 1940), 2.3 (Barker, 1948), 2.6 ± 1.08 and 2.9 ± 0.39 (standard error of mean) (O'Neal & Heinbecker, 1953). 2.8 (Carr, Beierwaltes, Raman, Dodson, Tanton,

Betts & Stambaugh, 1959), 2.6 (Kaneko, 1960), 3.6 ± 0.24 in the month of March and 6.2 ± 0.57 in October (Kelsey et al., 1960), 2.5 - 7 (Kaneko, 1963), up to 6.5 (Kral & Schwartzman, 1964), 2.0 ± 0.25, 1.99 ± 0.24, 1.05 ± 0.24 (Theran & Thornton, 1966), 1.3 - 1.8 with a mean of 1.6 (Hollander, Thompson, Barrett & Berlin, 1967), range 1.4 or 1.5 - 3.5, mean 2.3 or 2.4 (Belshaw, 1967; Siegel & Belshaw, 1968; Siegel, 1971), 3.2 ± 1.25 (Frey, 1967), range 1.5 - 5.1 mean 3.4 ± 1.05, and mostly between 2.4 - 4.38 (Mallo & Harris, 1967), range 1.1 - 4.3, mean 2.3 ± 0.8 in male dogs and 1.2 - 3.0, mean 2.1 ± 0.5 in female dogs (Quinlan & Michaelson, 1967), 2.11 ± 1.33 (Thomson & Michaelson, 1967), 3.7 ± 1.2 (Furth, Becker, Nunez & Reid, 1968), range 0.7 - 2.3, mean 1.4 ± 0.5 (Rijnberk & Vanderhorst, 1969), range 1.2 - 3.6, mean 2.4 ± 0.6 (Muller & Kirk, 1969), 2.0 ± 0.5 (Bullock, 1970), range 0.9 - 8.2, mean 2.8 ± 1.3 and range 0.9 - 8.2, mean 2.4 ± 0.7 for two overlapping groups of dogs (Bush, 1970a), 1.8 - 4.5 (Kaneko, 1970), 1.6 - 7.5 (Refetoff et al., 1970), 1.55 (Anderson & Dorner, 1971), range 0.7 - 2.9, mean 1.9 ± 0.65 (Rijnberk, 1974), 1.6 - 3.0 (Baker, 1971), 1.0 - 5.0 (Farran & Bush, 1971), range 2.3 - 4.0, mean 3.0 ± 0.5 (Bush, 1972b), 2.4 ± 0.6 (Belshaw, Barandes, Becker & Berman, 1974) and 1.5 - 2.5, 92 per cent of euthyroid dogs having values over 2.2, (Lorenz & Cornelius, 1976; Muller & Kirk, 1976).

Hypothyroid dogs. The PBI values in hypothyroid dogs have been similarly reported (in mcg/100 ml plasma) as follows: 1.0 on the fifth day following hypophysectomy (O'Neal & Heinbecker, 1953), 2.6 would be in the hypothyroid range (Kaneko, 1960), 3.0 in a hypothyroid bitch (Hoffer, 1962), 1.00 $\pm$ 0.25 and 1.6 would be marginally in the normal range but a case of hypothyroidism could have this value (Theran & Thornton, 1966), in thyroidectomised dogs it was 0.5 - 1, mean 0.8 (Hollander et al., 1967), it is usually below 1.0 and is rarely more than 1.4 (Belshaw, 1967; Siegel & Belshaw, 1968), 1.0 $\pm$ 0.5 (Muller & Kirk, 1969), 1.1 $\pm$ 0.5 (Bullock, 1970), below 1.8 indicates hypothyroidism (Kaneko, 1970). Thyroidectomised dogs have a value of 0.83 (Anderson & Dorner, 1971), 0.6 - 1.6, 93 per cent of hypothyroid dogs having values below 2.2, (Lorenz & Cornelius, 1976; Muller & Kirk, 1976).

IN VITRO UPTAKE BY RED BLOOD CELLS OR RESIN OF RADIO-ACTIVE IODINE LABELLED TRIIODOTHYRONINE

Introduction

As has already been discussed, circulating thyroid hormones, T4 and T3, are mainly bound to globulin. When the amount of globulin is normal and the thyroid hormone level is low, a related number of the globulin binding sites are unoccupied. If thyroid hormone is then introduced into the blood stream, the unoccupied globulin sites will take up the fresh supply of hormone and bind it. This is the basis of an in vitro test in which a measured amount of triiodothyronine, in which the iodine has been radioactively labelled (*I-T3), is added to a whole blood sample.

The unoccupied globulin binding sites take up a proportion of the added T3 and some surplus is left. The RBC, because their avidity for thyroid hormone is less than that of the globulin, bind the surplus to their surfaces. If the RBC are now separated from the rest of the blood sample and their radioactivity measured, it will be ascertained whether they have taken up little or much of the *I-T3. If they have taken up little, this indicates that much has gone to the globulin, showing that there were many unoccupied globulin binding sites originally, i.e. a state of

hypothyroidism. If much radioactivity is measured in the RBC this indicates that the globulin sites were already occupied as is the case in euthyroidism or hyperthyroidism. The amount taken up by the red cells is given as a percentage of the original radioactivity, and a high RCU percentage indicates euthyroidism or hyperthyroidism, whereas a small percentage uptake reflects hypothyroidism

A development of the technique is one in which the RBC are not used, a plasma sample only being utilised and a substance such as a resin added to replace the RBC. The resin's avidity for *I-T3 is less than that of the TBG so the test works in the same way as the RCU test.

The amount of radioactivity attached to the resin, after it has been separated from the serum is measured. Thus the test has become known as the T3 resin uptake test or resin T3 uptake test (resin T3U, RT3U or T3U). The test using whole blood is referred to as the red cell T3 uptake test (RCT3U) or erythrocyte T3 uptake test (ET3U).

The results are still expressed as a percentage of the *I-T3 added. The test has caused confusion amongst some workers who, by referring to it as the T3 test, have appeared to imply that it measures T3 in the circulation. In fact, it only indicates the extent of free TBG. Since the main circulating thyroid hormone is T4, the test is an indicator of how much of the TBG

is already occupied by T4. That is, it is an indirect way of assessing circulating T4.

This summary of the principle underlying the T3 uptake test is followed by a review of the literature dealing with its evolution, usefulness and results obtained by it.

Literature Review

The uptake or binding by the human red blood cell of radioactive ^{131}I - labelled triiodothyronine (^{131}I-T3) is consistently greater than its uptake of ^{131}I - labelled thyroxine (^{131}I-T4) and the presence of plasma markedly decreases RBC uptake of ^{131}I-T4 and, to a lesser extent, that of ^{131}I-T3 (Crispell, Kahana & Hyer, 1956). From this knowledge, Hamolsky, Stein and Freedberg (1957) developed the method of in vitro incorporation by the human RBC of ^{131}I-T3 added to the whole blood, referred to in the introduction. They counted the radioactivity in the separated, washed RBC, as a percentage of whole blood radio-activity, corrected to a haematocrit reading of 100. They studied the effect of various factors on the test. The addition of non-thyroid organic iodine-containing compounds caused either no change or a slight increase in uptake. Pregnancy or the oral administration of propyl-thiouracil decreased erythrocyte uptake (RCU). Nephrosis, hepatitis, hepatic cirrhosis, extensive metastatic malignancy and administration of

dicoumerol increased RCU. Hamolsky, Golodetz and Freedberg (1959) referred to its value as an in vitro test, possessing diagnostic accuracy in man comparable to other standard methods. It was especially useful after a patient had received organic iodine compounds as they did not interfere with the results. Also, it was useful in monitoring the effects of therapy in hypo- and hyperthyroidism. To the list of factors affecting the uptake, they added that the uptake is decreased by administration of oestrogen and is increased in pulmonary insufficiency with CO_2 retention, paroxysmal atrial arrhythmias and following the administration of anticoagulants.

Wilson, Dickson and Frost (1961) noted that the Hamolsky method utilised the RBC as secondary binding sites and reported that of the species of animals tested, horses and dogs diagnosed as hypothyroid, possessed the lowest uptakes. Three clinically hypothyroid dogs had a mean value of 11.12%, the lowest being 9.25% and the highest 12.80%. The normal was 11.0 and 29.0% (mean 18.34%) indicating an overlapping of values.

Shapiro and Rabinowitz (1962) and Rabinowitz, Shapiro and Johson (1963) used the RT3U test and found it to be as statistically reliable as Hamolsky's RCT3U method as an aid in diagnosing the thyroid status in man. The advantages of the method they used were that it eliminated the need to wash RBC, excluded complications due to haemolysis and did not require the use

of a haematocrit correction factor. It did, however, require a correction for free iodide. Rabinowitz, Banks and Greenberg (1964) measured RT3U in beagles, on a standard diet, over a 6 week period. Normal and thyroidectomised dogs and thyroidectomised dogs made euthyroid by the administration of L-triiodothyronine orally, were tested. They found that the initial control values of dogs of the same sex, age and breed were significantly different from one another, making any valid comparison of their collective mean value impossible. They concluded that the establishment of valid values representing hypo-, eu- and hyperthyroid levels in dogs required further investigation. They considered that reliable values might never be obtained due to the possibility of wide breed variations. However, they suggested that the RT3U test would be of use to veterinarians to make a preliminary evaluation of the thyroid status of dogs showing clinical signs of suspected thyroid malfunction.

Greve and Gaafar (1964b) used the RBC uptake test in 18 dogs before and after thyroidectomy. Pre-ablation values of from 5% to about 25% uptake with the majority between 11 and 13%, were obtained. Seven to ten days post-operatively, the average value was about 8%. They found that subsequent individual RCU values were erratic. Like Wilson et al. (1961), they observed an overlapping of single values but found that a series of 3 or 4 determinations indicated the

proper state of thyroid function. (It is evident from a personal communication of Belshaw, 1962, to Greve and Gaafar, that Belshaw was already using the RCT3U method). Munson and Belshaw (1966-67) considered that the use of the RCT3U test had been limited, and its diagnostic value remained in doubt until more experience had been gained of it with hypothyroid patients.

Mallo and Harris (1967) noted that RCU procedures had been used on human and canine blood in vitro and that a modification of the method using resin instead of red blood cells had been introduced in human medicine. They cited the following, in respect of resin uptake in man, Mitchell, Harden and O'Rourke (1960), Sterling and Tabachnick (1961), Godden and Garnett (1964) and Goolden, Gartside and Orsorio (1965). The resin uptake method did not require haematocrit correction and it was as accurate, in man, as other procedures in use. Accordingly, Mallo and Harris applied it to the dog, using a commercially available kit (Abbott Laboratories, Illinois). The polyurethane resin is embedded in a sponge. In 30 clinically euthyroid dogs, the T3 resin sponge uptake test range was 34.4 - 57.3% (mean 49.9%). Taking $\pm$ 1 standard deviation as the normal range for this series, the range was 44.0% to 55.8% uptake. If the range is extended to 42% to 57% uptake, this would include 92% of the values obtained. In fact, 63.3% fell within the mean $\pm$ 1 SD, 20% were lower and 16.7% were above this. No sex, breed or age differences were seen. However,

they note that two young female dogs had high T3 uptake figures in association with high PBI levels, suggesting that in their cases, normal amounts of thyroid hormone were present but an excess of binding sites was available. These animals were at the age of puberty when an increase of oestrogen may be expected. Nonetheless, a similar feature was not observed in 6 other females of the same age and they suggest that there may be individual biological differences.

Ekman, Orstadius and Thorell (1968) used the red blood cell ^{131}I-T3 uptake test on 48 apparently normal dogs of 15 breeds, the sexes being equally represented, and obtained RCU of 36.5 $\pm$ 4.5%. The same test showed that dogs with alopecia and dogs with adiposity had statistically significantly lower RCU values (and statistically significantly higher serum cholesterol values) than the normal dogs. They omitted cases of Cushing's disease or alopecia associated with gonadal dysfunction. There was no statistical difference from the normal RCU value in dogs with acanthosis nigricans, which suggested that this condition cannot be regarded as hypothyroidism. They state that their results cannot be compared with those of Wilson et al. (1961) because of differences in technique.

Kallfelz (1968) used the T3 resin sponge method (RT3U) and considered it to give a reliable indication of thyroid function in the dog and regarded it as applicable in practical veterinary medicine. The normal RT3U value for dogs was 42 - 48%. Later, however, he (Kallfelz,

1969a) compared RT3U with T4CPB and found the former relatively insensitive and the latter very sensitive to induced increases in thyroid function in 6 dogs and to naturally occurring decreases in function in two. He noted that the RT3U was an indirect test and it gave erroneous results when the serum protein level was abnormal or the albumin:globulin ratio was altered. Accordingly, although T4CPB was the more complicated and expensive, he preferred it for the precise determination of T4 and suggested the use of RT3U for screening. If a suspected hypothyroid case gave a RT3U value in the normal range, it would be wise to conduct a T4CPB. In this paper he gives the normal RT3U range as 42 - 60%, and in 2 suspected hypothyroid dogs as 36.3% and 48.3% respectively. In 15 euthyroid dogs he (Kallfelz, 1969b) found the RT3U to be normal, with a mean of 51% $\pm$ 3.5 SD, but poorly correlated with T4CPB results.

Hightower and Miller (1969) described the resin sponge (RT3U) and red blood cell (RCT3U) uptake tests using radio-active labelled T3 and warned that before comparing reported results, the procedure used should be noted. RCT3U values were lower than those for RT3U. Hightower, Miller and Kyzar (1969) reported RT3U (Trisorb, Abbott Laboratories) results on 148 dogs. Of these, 118 (80%) gave results from 44 - 58% uptake and they regard this as constituting the normal or euthyroid range. The hypothyroid "grey area" is 40 - 43% and below 40% is regarded as being indicative of

hypothyroidism. The hyperthyroid "grey area" is 59 - 62%. Although they had obtained results above this, they had not observed a "true clinical hyperthyroid animal". They discuss factors affecting the test results in man. In addition to factors previously noted in this review, they mentioned that salicylates, phenylbutazone, testosterone and androgens increase the uptake. Any situation in which circulating thyroid hormone concentrations or TBG levels are altered, or substances which compete with thyroid hormone for binding sites are present, can result in what they describe as a "suspicious" test. The two conditions in animals they had observed to affect the uptake test were pregnancy and an abnormal serum protein electrophoretic pattern. Generally, while the results of one kind of thyroid function test may occasionally suffice, they recommend that several tests be used and consider that the RT3 uptake, T4 assay (CPB) and serum cholesterol quantitation appear to be satisfactory for most cases.

Quinlan, Thomson and Michaelson (1969) found that analyses of the percentage RT3U in 78 dogs revealed no correlation with age or PBI values. Reid (1969) regarded it as unreliable in determining canine thyroid function.

Bush (1970a) using the RT3U test (Trisorb test kit, Abbott Laboratories) found no correlation between the values obtained and the breed of dog investigated. He found that dogs with an uptake of 45% or less were twice as likely to be hypothyroid as euthyroid while

those with values below 42.5% were almost sure to be hypothyroid.

Bustad and Fuller (1970) referred to the advantages that the RT3U test had over the assay of PBI, in that the former was not affected by iodine contamination but they considered that total serum proteins should be determined in conjunction with the test.

Refetoff, Robin and Fang (1970) give RT3U results for 3 dogs as 51.7%, 57.6% and 56.0% respectively. Anderson and Dorner (1971) misleadingly referred to T3 uptake tests as T3 assays, but did however refer to the results in percentage uptake terms. They report for 11 normal and 12 thyroidectomised dogs, mean RT3U values of 51% $\pm$ 5.3 SD (range 41 - 61%) and 47.9% $\pm$ 7.1 SD (range 34 - 60%) respectively and note that, compared with the T4 assays conducted on these dogs, the RT3U test lacks sensitivity.

DiScala, Lippe and Segal (1971) found that the RT3U test gave significantly different ($P = < 0.001$) results in normal dogs and dogs with induced hypothyroidism. Fourteen control dogs and 6 hypothyroid dogs had RT3U mean values of 54% $\pm$ 5.1 SD and 39% $\pm$ 6.2 SD respectively. Thus they considered it to be a reliable index of hypothyroidism in the dog.

Orstadius (1971) reviewed the situation to date in Sweden noting, with regard to the red cell T3 uptake test, that he and his colleagues (Ekman & Thorell, 1965; Ekman & Orstadius, 1966; Ekman et al., 1968) considered it a valuable method of estimating canine thyroid function.

In 60 dogs suspected of hypothyroidism on clinical grounds, i.e. mainly because of dermatosis, 17 were shown to be hypothyroid with low RCT3U values (and most of them had elevated cholesterol values also). Other disorders were diagnosed in the other cases by a variety of means, indicating the importance of conducting laboratory tests on suspected hypothyroid cases.

RT3U values are higher in dogs than in man (Rijnberk, 1971). A low RT3U value (37.1%) and elevated serum cholesterol value (524 mg/100 ml) indicated hypothyroidism in a dog. Rijnberk (1971) regarded the RT3U as a specific indicator of canine thyroid function.

In euthyroid dogs the RT3U values were: mean 48% $\pm$ 5 SD (range 41 - 55%) (Siegel, 1971).

In non-pregnant bitches, RT3U (Trisorb-131, Abbott Laboratories) values of 42% or less are almost conclusive proof of hypothyroidism (Bush, 1972a). In 16 euthyroid dogs, Bush (1972b), using the RT3U test (Trisorb-131, Abbott Laboratories) reported a range of 50.6 - 59.7% (mean 54.3% $\pm$ 2.0 SD) and indicated that these values were slightly higher than those reported by others, e.g. 49.9% (Mallo & Harris, 1967) and 49.6% (Kallfelz, 1968). He notes that when the lowest of the values reported by Mallo and Harris (1967) are excluded, their RT3U range is virtually identical with that of Kallfelz (1968). The lowest values were for dogs under one year old. He regards the RT3U test as a very convenient screening method for checking the thyroid status of dogs and,

with the in vivo thyroidal uptake test and PBI, to be amongst the most valuable.

Kyzar, Chester and Hightower (1972) compared a number of tests in euthyroid and known hypothyroid dogs. The RT3U test was not as accurate as the T4 assay and many of the clinically hypothyroid dogs gave RT3U values within the euthyroid range.

Solomon, Benotti, DeGroot, Greer, Pileggi, Pittman, Robbins, Selenkov, Sterling and Volpe (1972) were appointed by the American Thyroid Association to develop a nomenclature to clarify the situation. The resin triiodothyronine uptake test may be referred to as RT3U and it includes all other non-cellular absorbing media, e.g. charcoal and sephadex. Other terms should be avoided because of the confusion already existing. Also attempting to regularise the terminology, McGowan (1975) used the terms ET3U and RT3U for the red blood cell (erythrocyte) and resin uptake tests respectively. In this review, the abbreviation RCT3U is retained for the red blood cell triiodothyronine uptake tests.

Kallfelz (1973) compared RT3U, over a 10 week period, in intact and thyroidectomised dogs and found that the RT3 uptake declined in the latter. He remarks that it had been reported (Anderson & Dorner, 1971; Kallfelz, 1969a) that T3 uptake was not responsive to changes in thyroid status. This matter, he states, requires further investigation. Kallfelz and Erali (1973) referred to the suspicion of DiScala et al. (1971) that the reason for experimental hypothyroidism by

thyroidectomy failing to bring about a change in the RT3U results could be that accessory functioning thyroid tissue remained. However, Kallfelz and Erali, bearing in mind the results obtained by Kallflez (1973) in his thyroidectomised dogs, considered the discrepancy to be only partly explained. Regarding the effect of age, they had previously noticed that serum T4 concentrations seemed to decrease with increasing age, i.e. thyroid function decreased with age. They investigated this matter by RT3U and T4CPB (= T4RIA), using commercial kits (Abbott Laboratories, Illinois) in 3 groups of 5 dogs. They reported RT3 mean uptake percentages of 44.7 $\pm$ 0.94, 44.2 $\pm$ 1.26 and 43.1 $\pm$ 2.72 in dogs aged 12 weeks, 1 year and 3 - 6 years respectively. These changes were not significant but the T4 assays did reveal a significant decrease in T4 concentration with increasing age. This suggested that RT3U may not be a sensitive indicator of canine thyroid function.

Mason and Wilkinson (1973) also considered that the RT3U test was unreliable as a direct measure of thyroxine.

Increasingly, it was becoming apparent that the RT3U test was requiring more interpretation than direct tests of thyroid function and that levels regarded to be within the normal range were found in hypothyroid dogs (Hightower et al., 1973a).

Hightower, Kyzar, Chester and Wright (1974) regarded the following RT3 uptake values helpful in assessing thyroid function in dogs: less than 40%,

40 - 43%, 43 - 45% being indicative of hypothyroidism, "grey area" of hypothyroidism and euthyroidism respectively. Six normal beagles tested over one year, had T3U values, at some time, in the hypothyroid or "grey area". The T4 assays they conducted also showed this effect. They concluded that a battery of tests was needed, rather than a single one. They (Chester, Hightower, Kyzar & Wright, 1974) continued their studies and found in 26 control beagles a mean RT3U value of 49.12% (± 3.46 SD). Post-radiothyroidectomy, the mean value for 20 dogs was 42.82% (± 3.2 SD). The range for controls was 35.7 - 57.8% and, for the thyroidectomised dogs, 30.6 - 55.6%. In the latter, 120 (43%) of 278 samples were above 43% uptake, a value considered as normal for the test kit used (Trisorb-125, Abbott Laboratories). These results, the authors state, cannot be compared with those obtained using other tests. They reflect the slow and incomplete RT3U reaction to changes in thyroid function. The RT3U alone is unsatisfactory for thyroid function assessment.

Kelley, Oehme and Hoffman (1974) evaluated a selection of commercial thyroid function tests in dogs, including two RT3U tests (A, Trisorb-125, Abbott Laboratories, and B, Trilute, 125-Col, Ames Company). Test kit A did not reveal sex differences whereas test kit B did, females having slightly higher values (mean 85.06% ± 4.97 SD) than males (82.7% ± 4.24 SD).

These differences were not statistically significant, nor were the differences between 0 - 6 month old pups and the total population tested. The mixed-breed dogs had significantly lower T3U (kit B) results than greyhounds and German shepherd-greyhound crosses, which suggests that breed differences in thyroid function exist, as has previously been reported by others (Nunez, Becker, Furth, Belshaw and Scott, 1970) and is implied by the breed incidence already referred to in this review. Their (Kelley & Oehme, 1974) further studies with RT3U (Trisorb-125, Abbott Laboratories) failed to reveal sex differences, or differences when serum or plasma was used. There was a significantly higher value in beagle puppies than in adults. Adult mixed-breed dogs had a non-significantly lower uptake value than adult beagles. These facts confirm their earlier findings.

Bold and Browning (1975) discussed the importance of quality control and inter-laboratory comparisons for in vitro thyroid function tests and Hoffenberg (1975) reviewed their role up to 1972 in man, noting that radio-immunoassays for T3 and T4 should soon be widely available. The consideration being that when such were in use, the indirect RT3U could presumably be dispensed with. Horn (1975) gives a detailed account of the evolution of the T3 serum uptake tests, with special reference to their use in man.

Capen, Belshaw and Martin (1975) considered that

there is no clear separation of T3 resin uptake values in normal and hypothyroid dogs and demonstrated this with a figure showing that most of their RT3U results for normal beagles lay about 45 - 60% and most of the values for hypothyroid dogs were between 42 - 52%. They suggest that although the test is useful in human medicine because the resin only serves as a passive binder for labelled T3 in human serum, in canine serum the resin behaves as an active competitor because of the weaker affinity of canine plasma proteins for thyroid hormone. Kraft (1975) states the T3RU in normal dogs is 41 - 49%. Munzer, Hartung and Blaurock (1976) give RT3U values for the dog as 47 $\pm$ 33% and they discuss the difficulties of determining normal values.

Lorenz and Cornelius (1976) recorded RT3U values for normal and hypothyroid dogs as 42 - 60% and 34 - 60% respectively. Following TSH stimulation, in normal dogs the value is 45 - 60%. Figures were not available for post-stimulation values in hypothyroid dogs. The RT3U test is not sensitive to changes in thyroid gland function in the dog because of the thyroxine binding proteins of the dog having a different affinity for binding labelled T3.

Although RT3U tests originally appeared able to distinguish hypothyroid dogs by an uptake of 42% or less, Bush (1977; 1978; 1979) considered that only values below 37% could be confidently identified as hypothyroid. Such values occur in only half of the cases. Possibly

the overlap of normal and hypothyroid ranges is due to individual variations in protein binding. About this time, medical scientists in Great Britain (Burr, Ramsden, Evans, Hogan & Hoffenberg, 1977) also reviewed their attitude to the value of RT3U tests, agreeing that although the results were highly reproducible, their sensitivity to change had not been critically evaluated. Accordingly, they compared a T3 uptake test (Thyopac-3, Radiochemical Centre, Amersham) and TBG concentration in healthy euthyroid people with widely different TBG concentrations. The indirect method (RTU3) was inaccurate when TBG concentrations were high. A direct measurement of thyroxine binding globulin would probably soon be available as a routine diagnostic aid in human medicine, and this would, they state, facilitate assessment of thyroid function.

The results of RT3U tests on the dog are too variable for the technique to be considered of significant diagnostic value (Kallfelz, 1977). The test is more accurate when combined with a direct method for quantitating thyroxine (Siegel, 1977).

Summary

It appears that the triiodothyronine-resin-uptake test is of limited value by itself in determining the state of thyroid function in the dog. Because of this, and the modifications employed by different workers, no

table or summary of measurements reported is presented here. A number of authors both in veterinary and human medicine have evolved an index by multiplying the RT3U percentage by the T4(RIA) or other thyroxine assay result in the same patient or experimental subject, in order to evaluate thyroid status. This is discussed later.

MEASUREMENT OF THYROXINE IN SERUM AND PLASMA

Pileggi, Lee, Gloube and Henry (1961) described a column chromatographic method of determining serum T4 concentration involving the use of the ion-exchange resin Dowex-1, which was intended to allow separation of T4 from the other, interfering, serum iodine constituents. Acetic acid column eluates containing the thyroxine were subjected to incineration to destroy the organic matter and the inorganic iodide was then assayed. The specificity of the procedure depended on the completeness of the separation of T4 from the other iodine constituents. T3 was not separated from T4 by this method but they considered that as T3 constitutes only 5% of the total T4 and T3 in human serum and as it is also physiologically active, its presence afforded no serious problem. However, Pileggi and Kessler (1968), noting that exogenous organic iodine compounds interfered with the reaction, modified the technique. They retained the columns, but excluded the incineration and used other halogens (bromide and chlorine) in pretreatment of the eluates. They obtained more specific results. The method is referred to as T4 by column (T4Col).

Murphy and Pattee (1964) described a procedure for thyroxine determination, based on the specific binding properties of thyroxine binding globulin(TBG),

which involved the use of ^{131}I labelled T4 and sephadex columns. They regarded the method as being highly specific for T4 estimations in man. Murphy and Jachan (1965) modified the method by using ion-exchange resin and dispensing with columns. They continued to extract the T4 from serum with organic solvents and still used ^{131}I-T4. Unlike the protein bound iodine (PBI) determination the competitive protein binding (CPB) method was not affected by iodine or mercury contamination. Except for radioactivity counting, it required no special equipment. The method became known as competitive protein binding or CPB or the Murphy-Pattee method and is referred to as T4CPB.

Kallfelz (1969a) measured total serum T4 in dogs using a CPB method which did not require prior extraction of the T4 by solvents or the use of columns. In this method the serum T4 is estimated from the amount of ^{125}I-labelled T4 released from labelled thyroid binding globulin (TBG) as the result of an interaction with the serum T4. He found the test very sensitive in both induced and naturally occurring hypothyroidism in dogs. Because of this sensitivity, which is greater than that of the T3 uptake test, he considered that the T4CPB test should be used if T3 uptake results were in the normal range in a suspected case, even although, in his opinion, the T4CPB was more difficult to perform than the RT3U test. He regarded the T4 test as the

one to use when distinguishing between primary and secondary hypothyroidism. He (Kallfelz, 1969b) stated that the circulatory T4 levels were also best measured in euthyroid dogs by this direct method. According to Kallfelz, the clinical significance of PBI, T4Col or T4CPB is the same as all are measurements of T4. He found the commercial kit Tetrasorb-125 (Abbot Laboratories) simple to use for the T4 estimations. It was not affected by exogenous iodine. Muller and Kirk (1969) also noted that exogenous iodine did not interfere with this test even when the T4 levels were low, but that diphenyldantoin (Dilantin), because of its strong selective binding to thyroxine-binding globulin, could interfere and give unexpectedly high results.

Reviewing the literature, Hightower and Miller (1969) noted that T4CPB measured the circulating level of total thyroxine. Hightower, Miller and Kyzar (1969) measured T4 by Tetrasorb (Abbot Laboratories) and found no difference in the levels in serum and plasma of the same animal. They used di-potassium EDTA (Sequestrene) as the anticoagulant when obtaining the plasma samples, and accepted that the effect of other anticoagulants on T4 tests had yet to be ascertained.

Bustad and Fuller (1970) considered that T4CPB being a simplified method, could replace the PBI test

but they referred to the opinion of Bush (1969b) that T4CPB may not be of particular value in the dog due to the presence of high levels of T3. They thought that, although both the RT3U test and the T4CPB utilised resin sponge systems, the procedure for T4 was more difficult. Their opinion was that T4 determination by gel filtration chromatography based on the saturation of TBG, in the method devised by Murphy and Pattee (1964) and developed by Cuaron (1969), appeared to be more reliable and economical than the resin sponge methods.

Kaneko (1970) discussed the determination of thyroxine by column chromatography (T4Col), i.e. the method of Pileggi et al. (1961), and by competitive protein binding (T4CPB), i.e. the method of Murphy and Pattee (1964). He concluded that the former was superior to PBI assay as it suffered much less from interference by inorganic or organic iodine compounds, although radiographic contrast media containing iodine would interfere with it (Kaihara et al., 1969). The advantage of T4CPB was that it was not interfered with by exogenous iodine contaminants such as contrast media but compounds, such as Dilantin or salicylates did interfere as they competed with T4 for the binding sites.

Refetoff, Robin and Fang (1970) conducted a variety of thyroid function tests including T4CPB on

a number of vertebrate species. They considered that T4CPB gave a more accurate index of thyroid status than did PBI.

The greater part of protein bound iodine consists of T4 (Acland, 1971) and most of the serum T4 is thus bound (Siegel, 1971). The total serum thyroxine test gave more meaningful results than PBI assays because, they considered, it was not affected by the presence of medications containing iodine. Although the earlier CPB method had this advantage, it was necessary to extract the T4 from serum with organic solvents and this might cause artefacts unless conducted above pH9 (Bellabarba and Sterling, 1969). The extraction procedure was eliminated by using whole serum in the improved thyroxine displacement or CPB test.

Anderson and Dorner (1971) determined serum thyroxine in dogs using a T3 uptake test and a T4CPB assay. They found the latter to be more accurate and more sensitive and thus preferred it. Also, contrary to the opinion of Kallfelz (1969a) and Bustad and Fuller (1970), they found that T4CPB was not more difficult to perform than the T3 uptake test, although it took longer. They considered, from their results, that in suspected hypothyroidism, T3 uptake values might be normal, whereas T4 values would be subnormal. They found also that fasting cholesterol levels corroborated the T4 results, but that the T3 uptake

results did not. Although these authors refer to "^{125}T3 assay", it is clear that they do not mean assay of T3 but the use of a T3 uptake test.

T4 by column (T4Col) is very efficient in the removal of inorganic iodide, iodoproteins and some other, endogenous, non-hormonal organic iodo-compounds such as monoiodotyrosine (MIT) and diiodotyrosine (DIT), and is easily adapted to routine laboratory use (Baker, 1971). Baker observed that inorganic iodide levels as high as 1000 mcg/100 ml did not interfere with T4Col determinations. However, when factors such as the administration of organic iodine-containing drugs invalidated the direct analysis of the hormone by T4Col, Baker preferred estimating T4 by CPB because it avoids interference from non-hormonal iodine and is independent of the protein T4 binding characteristics of the plasma sample tested. He thought that the CPB method would be useful for measuring T4 in canine plasma as Dilantin is the only medicament known to interfere with the test.

Farran and Bush (1971) estimated hormonal iodine by a modification of the CPB column method and by a chemical method. In 4 normal dogs, they found that the percentage of T4 which was dialyzable was approximately 5 times that found in man by Hollander, Thompson and Barrett (1967). This would seem to explain the lower canine PBI values. The existence of a relatively

higher proportion of T3 in some dogs as compared with man could also provide an explanation for the lower canine PBI levels. Since in mammals T3 is 3 to 5 times more active biologically than T4, it would be possible for a dog having a higher proportion of T3 to obtain the same biological effects from a smaller amount of thyroid hormone (Gross and Pitt-Rivers, 1952b, 1953b; Pitt-Rivers and Tata, 1959).

Rijnberk (1971) regarded the diagnosis of thyroid disease in the dog as being hampered by the low level of circulating thyroid hormone which was difficult to estimate accurately and he noted that, as the estimation of total serum thyroxine by T4CPB had at that time been performed only in normal dogs (Kallfelz, 1969b), its clinical evaluation was still required.

At this stage it had become apparent that the multiplicity of tests had led to confusion in their names. For example, thyroxine (T4) iodine measured by column chromotography was regularly reported as "serum thyroxine by column" whereas it only measured 65% of the T4 molecule (i.e. its 4 iodines) and thus had a much lower range than serum thyroxine and, additionally, was susceptible to artefactual elevation by iodinated compounds entirely different from the thyroid hormone. In fact, physicians spoke of "the T4 test" although only T4 iodine may have been measured. Solomon, Benotti, DeGroot, Greer, Pileggi, Pittman,

Robbins, Selenkow, Sterling and Volpe (1972) thus considered that it was often difficult to know what had been measured by other workers and what calculation had been used to derive the figure reported as an index of free T4 concentration in serum. Accordingly, they suggested names for T4 tests as follows:-

a) Thyroxine (chromatographic), abbreviation T4(C); the test actually measures iodine which is usually reported as mcgI/100 ml. It is calculated as T4I/0.65.

b) Thyroxine (displacement), abbreviation T4(D); T4 is actually measured and reported as mcg/100 ml. Often it is called "Thyroxine (Murphy - Pattee)". Displacement refers to the group of methods described as displacement analysis, isotope displacement assays, saturation analysis, CPB and radio-ligand binding.

McGowan (1975) added T4(RIA) to the above to indicate assay of thyroxine by radioimmunoassay, for although it is a sub-type of displacement assay, it has unique characteristics and importance. In this thesis it is referred to as T4RIA.

Kyzar et al. (1972) considered that no single one of the many tests available was the best in all situations and conducted thyroid function tests using

T3 uptake, T4 assay and the in vivo ^{131}I uptake in dogs. Their results agreed, they state, with those of Kallfelz (1969a). The results of T4 assays and of ^{131}I uptake in vivo tests agreed in each case, and they also supported the clinical impression of euthyroid or hypothyroid states.

Lee, Tietz and Martinez (1972), Stein and Price (1972), Scherzinger and Grosser (1973), Hightower, Kyzar, Chester and Wright (1973_a) and Schalm (1975) preferred the CPB modified method to estimating PBI for the computation of T4. Manning, Corwin and Middleton (1973) also estimated serum T4 by CPB because of its sensitivity when serum T4 levels were low, as in canine hypothyroidism.

Kallfelz (1973) investigated changes in canine thyroid function caused by exogenous thyrotropin administration or thyroidectomy, using commercially available kits (Trisorb 125 and Tetrasorb 125, Abbot Laboratories) for the CPB method. Kallfelz and Erali (1973) conducted further tests on 7 species of domesticated animals and concluded that the RT3 uptake test was not sensitive in detecting changes in thyroid status and that the T4 assay test alone would be as valuable as the free thyroxine index in the dog. However, Blakemore (1974) disagreed with this view as he considered that canine T4 test results required considerable interpretation and were not especially

useful for establishing a diagnosis of hypothyroidism. Goldie, Jennings and McGowan (1974) examined the method of estimating T4 by CPB stage by stage and found that proteins as well as T4 were extracted, so producing inaccurate results. They proposed a modified method of increased accuracy and precision.

As most methods of measuring T4 use the CPB principle, Havard (1974) stated that to determine the fraction of T4 bound to protein, it must be separated from the free T4 by adding a secondary binder such as a resin or sephadex. This analysis had been adapted for use in commercial kits of which at least 6 were available.

Rijnberk (1974), noting that no single test had proved completely reliable in the diagnosis of thyroid disorders in the dog, recommended that at least 2 independent tests directly related to the thyroid function should be used and, if the result of one of these tests was equivocal, additional diagnostic procedures should be used. He considered that T4 by column results could be affected by iodine contaminants to some slight degree and, also, the method was imprecise for values below 1 mcg/100 ml. T4CPB was not affected by iodine contamination but the CPB methods, as then performed in commercial laboratories, were not accurate at the low T4 levels which occur in the dog. Thus further modifications were needed to achieve the necessary

accuracy. Rijnberk referred to the measurement of T4 and T3 by radioimmunoassay which had become available and thought that this could be promising but needed further clinical evaluation. His view was that T4Col in serum mainly represents T4 bound to TBP and closely reflects the total thyroxine in serum but that, however, a prerequisite for good diagnostic accuracy of the calculation was an exact determination of total serum thyroxine. Despite the qualifications he had made about them, he regarded the RT3U and T4Col tests as the most suitable at that time.

Serum T4 assays can be divided into two groups, chemical and radioisotopic. Clark (1975), speaking in 1972, reviewed the chemical methods and acknowledged that when the measurement of hormonal iodine was by conventional chemical means, the results were subject to invalidation by the presence of non-hormonal iodine. In radioisotopic methods (saturation analysis), the proteins may be naturally occurring as the TBG and, as such, are utilised in the CPB (displacement) assay. Extraction of hormone from serum is usually necessary. The eventual separation of the bound from the free fractions may be carried out by ion-exchange resin, dextran gel or charcoal. Commercial T4CPB kits were available, and were the most commonly used. Clark referred to the relatively recently introduced radioimmunoassay methods (RIA) for T4 determination in

unextracted serum. Although they were still being evaluated, they appeared to offer diagnostic accuracy and specificity.

According to Kaneko, Baker and Mills (1975), previously the most common approach to thyroid function tests had been to measure the level of serum thyroxine (T4) and in equivocal cases, to measure serum T4 response to exogenous TSH administration. They indicated that the principle of radioimmunoassay (RIA) is based upon specific antigen-antibody reactions, in vitro, with one of the reactants, in this case the antigen (T3, T4 or TSH), being radio-labelled for sensitive quantitation purposes. After binding to the specific antibody, either the unbound or the bound antigen is separated and its radioactivity measured. They also referred to the very low levels of thyroid hormones in the blood of domestic animals, which have been mentioned as being a major concern in clinical laboratory diagnosis, particularly since hypothyroidism is the most frequently encountered form of thyroid diseases in animals. They found no significant differences between the T4RIA and T4CPB values.

Marsden, Facer, Acosta and Howorth (1975) measured T4 in unextracted human serum by a modification of the RIA method of Mitsuma, Nihei, Gershengorn and Hollander (1971) and found excellent correlation with an established T4CPB method. They concluded that RIA had advantages of sensitivity, precision, simplicity and low cost.

However, Capen, Belshaw and Martin (1975) considered that the methods for T4 measurement in human sera were not sufficiently precise for accurate diagnosis in the dog. However, diagnostic accuracy could be obtained by modifying the procedure or by using larger volumes of test serum. These modifications are not routinely available in commercial diagnostic laboratories.

Lorenz and Cornelius (1976) noted that T4Col gave better results than PBI assay but was still subject to interference from some radiographic dyes and disophenol, and had been largely replaced by T4CPB. Lorenz and Cornelius considered T4CPB to be sensitive in detecting changes in thyroidectomised dogs. Their view of T4RIA was that it was similar in principle to the CPB technigue except that the specific T4 binding protein was replaced by an antibody specific for T4. Since T4RIA is so sensitive it requires only small quantities of serum and thus, they considered, it might have merit when dealing with cats and small dogs. Although at that time normal T4RIA values had not been published for the dog and cat, their limited experience of it suggested that the values obtained were similar to those determined by the CPB method.

Muller and Kirk (1976) considered that hypothyroidism was the most frequently misdiagnosed endocrine disease of dogs as the tests usually employed by veterinarians for thyroid evaluation were inappropriate since they did not reliably distinguish between hypothyroid and

euthyroid dogs. Although a single, accurate measurement of serum T3 or T4 would establish a diagnosis, most laboratories used methods which did not have this degree of diagnostic accuracy, because they were standardised for the range of values normally found in man. The lower limit of normal serum T4 in man is about 5.0 mcg/100 ml while in dogs it is about 0.8 mcg/100 ml. They noted that the procedures had been suitably modified both in the case of column chromatography (Rijnberk, 1974; Belshaw, 1975) and RIA (Belshaw, 1975; Davies, 1975). Muller and Kirk considered that until these suitable procedures for measuring canine serum T3 and T4 were generally available for veterinary practitioners, the routine method of evaluating canine thyroid function should be that of Bullock (1970) for determining the response of the thyroid to exogenous TSH administration.

Premachandra (1976), Premachandra and Ibraham (1976) and Premachandra and Lang (1977) measured canine plasma T4 and T3 levels by RIA.

Belshaw and Rijnberk (1977) considered that of the many direct and indirect tests available only the measurement of T4 or T4I by column chromatography, and the measurement of T4 and/or T3 by RIA are sufficiently sensitive and accurate for diagnosis of hypothyroidism in the dog. They have to be suitably modified to take account of the low hormone concentrations in hypothyroid dogs. The correlation of results between the

methods is excellent and a single measurement of plasma T4Col or T4RIA, or of T3RIA gave excellent separation of hypothyroid from euthyroid dogs.

Kallfelz (1977) regarded T4CPB as superior to RT3U as it is a direct indication of thyroxine level and thus of thyroid status. Furthermore, it is not affected by alterations in the serum protein level of the patient. It is also superior to PBI chemical determination because it is not affected by other iodine containing compounds. The T4RIA gave similar results to those obtained by T4CPB, although there may be less variability with T4RIA. The T4RIA results might be about 40% lower than those of T4CPB on the same sera.

Others have also conducted T4RIA evaluations. Their numerical results are given later.

Belshaw and Rijnberk (1979) discuss fully the advantages of using T4RIA and T3RIA in the dog and concluded that T4RIA and T3RIA were of about equal value in distinguishing between normal dogs and dogs with primary hypothyroidism, but that it was necessary to ensure that the method used was accurate for T4 levels well below 1.0 mcg/100 ml in the dog. They found that the RIA methods devised for use in human medicine required no major change for use in canine medicine. However, since the T4 range in canine plasma is lower than that of human plasma, it is essential that the hormone-depleted plasma added

to the control tubes and standards should have a T4 concentration that is negligible with respect to the lowest canine standard. They satisfactorily obtained hormone-depleted plasma by extracting that of hypothyroid dogs by charcoal.

Serum Thyroxine (T4) Concentrations Reported in the Literature

T4 Concentrations in Man

In man, Murphy and Pattee (1964) reported a mean value of thyroxine iodine (TI) for euthyroid subjects of 6.6 ± 1.3 mcg/100 ml (range 4.0 - 9.2) corresponding to a mean thyroxine (T4) level of 10.1 mcg/100 ml (range 6.1 - 13.8). In hypothyroid patients, the mean TI value was 1.81 ± 0.96 mcg/100 ml (range 0.3 - 3.8) and the mean T4 value was 2.75 ± 1.47 mcg/100 ml (range 0.4 - 5.8). Murphy, Pattee and Gold (1966) reported T4 mean values of 6.36 ± 1.64 mcg/100 ml and 6.60 ± 1.58 mcg/100 ml in euthyroid men and women respectively. They regarded T4 values of 4 - 11 mcg/100 ml serum as the normal human range. There are many later reports of T4 values and of thyroxine iodine values in man. The following results refer to the dog only.

T4 Concentrations in the Dog

T4 Concentrations by Column and by Competitive Protein Binding

Hollander, Thompson, Barrett and Berlin (1967) determined T4Col for normal and hypothyroid dogs and found that they were strikingly altered in the latter. They concluded that even although T4 values in the normal dog are quite low, the cholesterol and T4 values together discriminate between normal and hypothyroid dogs. They report mean T4 values of 1.2 ± 0.48 (S.D.) mcg/100 ml serum for normal dogs and 0.9 ± 0.05 mcg/100 ml serum for hypothyroid dogs. The values for T4 were not significantly altered following dinitrophenol administration in 2 normal and 2 hypothyroid dogs. They also administered L-thyroxine to hypothyroid dogs. The mean value of T4 before treatment was < 0.5 mcg/100 ml and afterwards it was 6.9 mcg/100 ml (range 4.1 - 10.2).

Kallfelz (1969a) obtained a mean T4CPB value of 4.34 ± 1.44 mcg/100 ml serum (range 2.59 - 6.79) in 6 adult beagles. In 2 dogs with suspected hypothyroidism the serum thyroxine levels were 1.07 and 1.87 mcg/100 ml. Kallfelz states the normal range is 2.10 - 6.50 mcg/100 ml. Kallfelz (1969b) reported the mean T4CPB in 15 euthyroid adult beagle dogs as 4.21 ± 0.96 mcg/100 ml (range 3.02 - 6.04). Thus, the 95% confidence limits for normal thyroxine values will be 2.29 - 6.13 mcg/100 ml.

Muller and Kirk (1969) quoted a personal communication by Kaneko (1969) that the tentative range for normal T4Col is 1.8 - 3.5 mcg/100 ml.

Hightower, Miller and Kyzar (1969) in interpreting the results of the T4 test (Tetrasorb, Abbott Laboratories) on canine sera, considered that hypothyroidism, "hypothyroid grey area" and euthyroidism were indicated by less than 1.0, 1.0 - 1.2 and more than 1.2 mcg/100 ml respectively. In 3 clinically hypothyroid dogs they reported T4 values as follows, dog 2: 0.92, 0.96, 0.77 mcg/100 ml; dog 3: 1.11 mcg/100 ml, and dog 35: 0.96 mcg/100 ml. In 36 normal dogs, the range was 1.8 to 3.82 mcg/100 ml.

Refetoff et al. (1970) reported T4CPB values in four dogs as follows:- 2.2, 1.4, 1.1 and 1.2 mcg/100 ml. Siegel (1971) reported a T4 range in euthyroid dogs of from 2.1 to 5.4 mcg/100 ml (mean 3.7 $\pm$ 1.0 S.D.)

Baker (1971) gave normal canine values by T4Col as 0.9 - 2.3 mcg/100 ml and by T4CPB as 1.4 - 2.1 mcg/100 ml.

In 8 normal and 12 thyroidectomised beagles, mean serum T4CPB levels (Tetrasorb, Abbott Laboratories) were 2.38 mcg/100 ml ($\pm$ 0.36 S.D.) and 1.27 $\pm$ 0.29 mcg/100 ml respectively (Anderson and Dorner, 1971). Also in clinically normal and in thyroidectomised beagles showing clinical signs of hypothyroidism, Kyzar, Chester and Hightower (1972) measured T4CPB

(Tetrasorb; Abbott Laboratories). In 6 normal dogs the T4 range was 1.36 - 2.14 mcg/100 ml and in 20 clinically hypothyroid it was 0.39 - 1.17 mcg/100 ml. The present writer, from the data of Kyzar et al., calculates means of 1.73 $\pm$ 0.32 mcg/100 ml and 0.8 $\pm$ 0.20 mcg/100 ml for the 2 groups.

Kallfelz (1973) used the same test kit (Tetrasorb; Abbott Laboratories) on sera from normal dogs. Four beagle dogs had values ranging from 2.28 - 3.12 mcg/100 ml (mean 2.74) and in another 4 dogs the range was 4.40 - 4.71 mcg/100 ml (mean 4.49). In 2 groups of 2 and 4 Labrador retrievers, the ranges were 2.32 - 2.38 mcg/100 ml (mean 2.35) and 1.13 - 3.61 mcg/100 ml (mean 2.36) respectively. Kallfelz and Erali (1973), also using the same test kit, reported mean T4 values in 3 groups of 5 normal dogs as 3.24 $\pm$ 0.51, 2.25 $\pm$ 0.35 and 1.49 $\pm$ 0.46 mcg/100 ml for dogs aged 12 weeks, 1 year and 3 - 6 years respectively. Total T4 concentration decreased significantly ($P < 0.01$) with increasing age.

Hoge, Lund and Blakemore (1974) measured serum T4CPB levels by Tetrasorb (Abbott Laboratories) in 19 clinically normal and 4 clinically hypothyroid dogs. The T4 range, in the former was 0.6 - 2.7 mcg/100 ml (mean 1.6 $\pm$ 0.70) and in the latter it was 0.8 - 1.1 mcg/100 ml (mean 0.9). The values for the hypothyrotic dogs were as high as or higher than the values for 7 of the 19 clinically normal dogs and they referred to the difficulty this causes

in diagnosis. They postulate that the response to TSH should be ascertained in dogs with low T4 values if the clinical signs are consistent with hypothyroidism.

Hightower, Kyzar, Chester and Wright (1974) estimated T4CPB (Tetrasorb, Abbott Laboratories) fortnightly for a year in 6 normal beagles and obtained the following results (presented as mcg T4/100 ml serum):

Dog No.	1	2	3	4	5	6
Sex	M	M	M	F	F	F
Range	1.01-3.14	1.21-2.45	1.25-3.04	1.20-3.39	1.20-3.19	1.25-3.33
Mean	1.62	1.95	2.10	2,06	1,92	2,02
SD	0.47	0.33	0.47	0.61	0.46	0.56

Chester, Hightower, Kyzar and Wright (1974) reported a mean serum T4 value in 32 dogs of 2.08 mcg/100 ml (± 0.48 S.D.), whereas following radiothyroidectomy of 26 of the dogs, the mean value was 0.95 mcg/100 ml (± 0.32 S.D.).

Kelley, Oehme and Hoffman (1974) used two different test kits, namely Tetrasorb-125 (Abbott Laboratories), and Tetralute (^{125}I Column T4 Test; Ames Co.) to measure T4 in serum and plasma of normal laboratory dogs. They did not find significant differences between the results in the serum and plasma or between the kits. The results were as follows (as mcg T4/100 ml serum):

Test	No. of dogs	Serum (± SEM)	Plasma (± SEM)
Tetrasorb (CPB)	24	0.94 ± 0.14	0.97 ± 0.16
Tetralute (Col)	30	0.96 ± 0.10	1.10 ± 0.11

Other results which they present for normal dogs are as follows (as mcg T4/100 ml):

Test	Breed	No.	Mean	S.D.	SEM
Tetrasorb	Adult beagles	8	1.20	0.57	0.12
	Beagle pups	39	2.27	0.59	0.09
	Mongrels	12	0.97	0.58	0.16
Tetralute	German shepherds	47	1.29	0.74	0.11
	Greyhounds	6	0.72	0.19	0.08
	GS x G	5	1.00	0.39	0.20
	Mongrels	11	1.05	0.42	0.21
Tetralute	Means	69	1.18	0.41	0.05

With Tetrasorb, they did not find significant sex differences. With Tetralute, they obtained significant differences for greyhounds compared with mongrels and for dogs up to 6 months old compared with the total sampled.

Kelley and Oehme (1974) measured T4 levels (Tetrasorb, Abbott Laboratories) and reported as follows:

			mcg T4/100 ml.		
Dogs	No. of dogs	No. & type of samples	Mean	SEM	S.D.
Adult beagles	8	23 serum	1.29 ±	0.13	0.63
3-9 weeks old beagles	39	39 serum	2.27 ±	0.09	0.59
Adult mongrels	12	12 serum	0.94 ±	0.14	0.49
	12	12 plasma	0.97 ±	0.16	0.56

The puppy beagles had significantly higher values than the adult beagles. The mean values they report are lower than those reported by others (Hightower et al., 1969; Kallfelz, 1969a,b; Anderson & Dorner, 1971, Kyzar, Chester & Hightower, 1972).

Kraft (1976) reported the mean plasma T4CPB in 520 normal dogs as 2.8 mcg/100 ml (range 1.4 - 4.7 mcg/100 ml).

Munzer, Hartung and Blaurock (1976) stated that the normal value for canine T4 was 1.2 mcg/100 ml. Kallfelz (1977) reported serum T4CPB levels as 1.19 $\pm$ 0.38 mcg/100 ml in hypothyroid dogs.

T4 Concentrations by Radioimmunoassay

Kaneko, Baker and Mills (1975) tentatively reported normal T4RIA results as 1.14 $\pm$ 1.52 mcg/100 ml, and T4CPB as 1.5 $\pm$ 1.3 mcg/100 ml and found no significant difference between them. T4RIA values in the dog are from 1.1 - 3.9 mcg/100 ml (Kraft, 1975).

Comparing results by different methods, Lorenz and Cornelius (1976) reported as follows (in mcg/100 ml):

	T4Col	T4CPB	T4RIA
Normal dogs	0.9 - 2.3	1.5 - 3.0	1.2 - 3.0
Hypothyroid dogs	< 0.5	0 - 1.7	<1.0

Premachandra and Lang (1977) reported T4RIA levels in canine plasma of from 0.2 - 2.4 mcg/100 ml (mean 1.4 ± 0.69). Sims , Redding and Nachreiner (1977) reported the T4RIA value in normal dogs to be 1.5 - 4.0 mcg/100 ml and in 2 hypothyroid dogs they were 0.47 ± 0.05 and 0.5 ± 0.01 mcg/100 ml respectively.

Chastain (1978) considered that the normal values for T4RIA range from 1.2 to 4.2 mcg/100 ml. In 9 normal dogs he found it to be 1.3 - 3.4 mcg/100 ml (mean 2.1 ± 0.77 S.D.) whereas in 4 clinically hypothyroid dogs, and one with a subnormal T4 baseline value, the range was 0.5 - 1.8 mcg/100 ml (mean 1.0 ± 0.48 S.D.). The means have been calculated by the present writer . The apparently normal dog with the low baseline T4 had a T4 level of 1.0 mcg/100 ml. It is interesting to note that one of the apparently clinically hypothyroid dogs had a T4 value of 1.8 mcg/100 ml which comes within the normal range of 1.2 - 4.2 mcg/100 ml, given by Chastain.

Reap, Cass and Hightower (1978) reported mean serum T4RIA values of 1.51 ± 0.38 mcg/100 ml (range 0.70 - 2.18 mcg/100 ml) in 10 dogs, all of which appeared normal and were believed to be euthyroid.

Belshaw and Rijnberk (1979) recommended that T4RIA values of 1.52 to 3.60 mcg/100 ml be regarded as normal.

Ihrke (1979) regards T4RIA values of less than 1.5 mcg/100 ml as diagnostic of hypothyroidism and values between 1.5 and 2.2 mcg/100 ml as falling in a "grey zone". Such cases, he says, should be handled according to the clinical impression.

Martin and Capen (1979) give 1 to 4 mcg/100 ml as the normal range of T4RIA in the dog and report below 0.8 mcg/100 ml as being usual in hypothyroidism.

Crispin and Barnett (1978), reporting in SI units, presented results of T4RIA in 5 normal and 5 spontaneously hypothyrotic Alsatians as 89.2 $\pm$ 1.71 nmol/l and 13.36 $\pm$ 1.12 nmol/l respectively, a highly significant difference ($P < 0.001$). The range for the hypothyrotic dogs was from 10.0 to 16.7 nmol/l.

Summary

It is not proposed to discuss the results of T4 by column or by CPB further, as these methods were not used in the present study. The results of T4RIA reported in the literature may be summarised as follows. The lower limit of the range in normal dogs is 1 mcg/100 ml and the upper is 4 mcg/100 ml. However, the lower end of the normal range overlaps with values found in some hypothyroid dogs to form a "grey zone" of values between about 1 mcg and 1.5 mcg/100 ml. Although according to Ihrke (1979) the grey zone

extends upwards to 2.2 mcg/100 ml, this is out of keeping with the values reported by others. Generally, values below 1.5 mcg or 1 mcg/100 ml are indicative of hypothyroidism.

MEASUREMENT OF TRIIODOTHYRONINE (T3) BY RADIOIMMUNOASSAY (RIA)

Development and Use of the Method

Eastman, Corcoran, Ekins, Williams and Nabarro (1975) reviewed the literature on the development of methods for assaying triiodothyronine (T3) in man. They stated that a significant advance in T3 assay methodology had resulted from the production of specific T3 antibodies by Brown, Ekins, Ellis and Reith (1970) and subsequently by the development of a sensitive and precise RIA for T3 (T3RIA) in serum extracts by Brown, Ekins, Ellis and Williams (1971). They stated that early attempts to measure T3 by RIA in whole serum were unsuccessful, mainly due to interference by endogenous thyroxine-binding globulin (TBG). Theoretically, it is possible to measure the T3RIA in the presence of TBG if the avidity of the antiserum for T3 greatly exceeds that of the TBG. In practice, however, this proved very difficult. The problem of TBG interference is overcome by using chemical compounds structurally similar to T3 which competitively inhibit binding of T3 to TBG. Eastman et al. (1975) discuss these various competitors for binding. They concluded that, although the concentration of T3 in serum, like that of T4, varied with changes in circulating TBG, T3RIA had proved to be a precise and reliable method for the detection of thyroid dysfunction in man. It was a valuable adjunct to the

assay for T4. Also, in man, Mitsuma et al. (1971) measured T3 in serum by both the RIA method and by a gas-liquid chromatographic technique in patients with primary or secondary hypothyroidism. The values obtained agreed closely and they concluded that T3RIA was sufficiently sensitive, precise and simple to permit its routine clinical application in man.

Knowledge of the development of the estimation of T3RIA in man was put to use in studying T3 in the dog. Farran and Bush (1971) compared the relative amounts of T4 and T3 in the blood of 9 apparently euthyroid dogs, using radioactive tracer and chemical methods. They remarked on the fact that, in some dogs, T3 may constitute a higher proportion of the circulating thyroid hormone than it does in man. Rijnberk (1971) referred to the T3RIA technique developed by Brown, Ekins, Ellis and Reith (1970), and indicated that it still needed clinical evaluation in the dog (Rijnberk, 1974).

Capen et al.(1975) considered that the method of Mitsuma et al. (1971) for the measurement of serum T3 was dependable in the diagnosis of canine hypothyroidism. They indicate that two factors should be noted. First, they recommend that, because of the diurnal oscillation in circulating thyroid hormone in the dog, the best separation between normal and hypothyroid dogs is obtained by measurements made about noon when the concentration in normal dogs is at its peak. Secondly, in iodine deficiency in the

dog, serum T4 values decline but T3 remains within its usual range. This is not, however, an important factor, as spontaneous iodine deficiency is rare in dogs in the United States. Belshaw, Cooper and Becker (1975) found that T3 levels were unaffected or only very slightly reduced by a large experimental reduction in the dietary intake of iodine. In dogs on a normal diet they found the T3 iodine concentration was about 4% of all the serum hormonal iodine, the remaining 96% consisting of T4.

Lorenz and Cornelius (1976) stated that although extensive measurements of T3RIA had been conducted in human medicine the results of similar evaluations in the dog had not, at that time, been published. Accordingly, the test remained to be evaluated in the diagnosis of canine and feline thyroid disease. They noted some reports from human medicine that, while in T3 thyrotoxicosis (hyperthyroidism) the test was of great value, this was not necessarily the case in hypothyroidism, where the T3 levels were not well separated from those of euthyroid subjects. Others (e.g. Eastman et al., 1975), on the contrary, had not encountered any human case of unequivocal clinical hypothyroidism in whom the serum T3 level was within the normal range.

Premachandra and Lang (1977) measured T3 by RIA as described by Premachandra (1976) and Premachandra and Ibrahim (1976). They obtained T3 values in normal

dogs similar to those obtained by Belshaw, Barandes, Becker and Berman (1974).

Kallfelz (1977) referred to the determination of T3 by RIA. A small fraction of circulating thyroid hormone is T3. It is secreted as such from the thyroid gland and also results from the deiodination of T4 at the tissue level. It is considered by some that T3 is the active form of thyroid hormone. Kallfelz remarks that T3RIA was originally developed for the diagnosis of thyrotoxicosis in man, in which hyperthyroidism is present due to elevated levels of T3 but not of T4. Because of the lack of published information comparing the values of T3RIA and T4CPB or T4RIA in canine thyroid dysfunction, Kallfelz undertook a preliminary trial. This failed to provide evidence that T3RIA was superior to T4CPB for the assessment of thyroid function in the dog, and he concluded that T3RIA may be of value only when used in conjunction with other techniques. He noted, however, that some other investigators were of the opinion that the serum T3 level was a better indicator of canine thyroid status than the measurement of T4.

Although the method of estimating T3 by RIA was available, Siegel (1977) considered that, because the physiological significance of T3 in the dog was not known, any values obtained would be of uncertain usefulness.

Reap, Cass and Hightower (1978) also referred to the lack of information about T3RIA values for comparative

purposes. Their own results indicated that T3 values fell into three levels, those being low in cats and horses, medium in dogs, cows, pigs and sheep and high in man, baboons and goats. The values were extremely high in rabbits.

As experience was gained, Bush (1978) suggested that the most valuable tests that could be performed were T3 and T4, by RIA, but that, at the time, a technique was not available in the United Kingdom which would produce accurate values for canine serum.

Martin and Capen (1979) considered that the RIA methods were the most sensitive, agreeing with Belshaw and Rijnberk (1979). Unfortunately, they remark, kits for T3RIA designed for human medicine are not always standardised or as sensitive as required to measure the lower levels of T3 in dogs, especially those with clinical hypothyroidism.

Although there is not a great deal of information about T3 levels and their interpretation, as yet, in the dog in a wide variety of circumstances, it is of interest that Scriba, Bauer,Emmert, Fateh-Moghadam, Hoffmann, Horn and Pickardt (1979) found T3 to be in the normal range in obese people. Furthermore, it was significantly higher than the mean for healthy controls of normal weight. The T3 level rapidly declined when the patients were totally fasted for a fortnight and it rose again during re-alimentation.

Published Values of Triiodothyronine

The following is a review of published T3 values. Various investigators have used different methods at different times.

Capen et al. (1975) published a diagram, illustrating the results of their investigation of T3RIA in adult beagles, which indicates that euthyroid animals had T3 from about 75 to 100 ng/100 ml serum with a cluster around 77 - 87 ng/100 ml whereas hypothyroid beagles had from about 40 to 70 ng/100 ml, with a cluster around 58 - 68 ng/100 ml. Belshaw, Cooper and Becker (1975) found normal T3 to be 83.9 $\pm$ 6.3 ng/100 ml (equivalent to 0.05 $\pm$ 0.003 mcg/100 ml for T3 iodine). Marked increases or decreases in dietary iodine had little effect. Only at intakes as low as 20 mcg iodine/day was there a significant decline ($P < 0.001$) in mean serum level and even these values were still clustered about the lower limit (72 ng/100 ml) of T3 observed in dogs on a normal diet.

Kaneko, Baker and Mills (1975) give a tentative normal value for T3RIA in the dog as 217 $\pm$ 45 ng/100 ml (mean $\pm$ SD). Kraft (1975) estimated T3RIA in 229 normal dogs and obtained a range of 20 - 206 ng/100 ml with a mean of 90 ng/100 ml.

Kallfelz (1977) stated that, while the results of T3RIA vary according to the technique used, preliminary figures for normal circulating T3 levels in the dog

were approximately 25 - 150 ng/100 ml. There was virtually no information on changes in level associated with age, breed and level of thyroid activity. Premachandra and Lang (1977) reported the mean T3RIA value for 15 dogs as 57 ± 21 ng/100 ml, with a range of 42 - 87 ng/100 ml.

In the dog, normal values for T3RIA are taken to be 75 - 200 ng/100 ml, by the Endocrine Diagnostic Laboratory of Auburn University, according to Sims, Redding and Nachreiner (1977) who report that in 2 hypothyroid dogs T3RIA values were 28.1 ± 8.2 ng/100 ml and 30.7 ± 0.5 ng/100 ml, respectively. Gosselin, Capen and Martin (1978) also agree that in canine hypothyroidism the T3 level is lowered.

In 10 normal dogs, Reap et al. (1978) recorded a T3RIA mean value of 96.2 ± 21.39 ng/100 ml (range 63 - 130 ng/100 ml).

Bush (1979) recommended that T3RIA be modified for use on canine serum because the T4 and T3 levels in normal dogs are much lower than those in man; they are even lower in hypothyroidism. T3 levels less than 50 ng/100 ml are found in hypothyroidism.

Belshaw and Rijnberk (1979), from their large investigation, record for diagnostic purposes that the normal range for T3 is 48 - 154 ng/100 ml, with a mean of 94 ng/100 ml. Martin and Capen (1979) regard 60 - 200 ng/100 ml to be the normal range for T3 and in dogs with primary hypothyroidism it is usually below 50 ng/100 ml.

Summary

It appears that in clinically normal dogs, T3RIA values range from about 50 ng/100 ml to between 100 and 200 ng/100 ml. Kraft (1975) and Kallfelz (1977) report levels in clinically normal dogs as low as 20 and 25 ng/100 ml, respectively. Typical means seem to be 83.9 ± 6.3, 96.2 ± 21.39, 90 and 96 ng/100 ml. The high mean of 217 ± 45 ng/100 ml (Kaneko et al., 1975) and the low mean of 57 ± 21 (Premachandra & Long, 1977) are outside the typical mean range.

The relatively few reports on the levels in dogs diagnosed as being hypothyroid give less than 50 ng/100 ml and include, e.g. 28 and 30 ng/100 ml. The data of Capen et al. (1975) suggest that most of their hypothyroid dogs have levels of 58 - 68 ng/100 ml.

Most who have studied thyroid function emphasise the need for each laboratory to decide on its own ranges for diagnostic purposes.

Using SI Units to report their results, Crispin and Barnett (1978) give the mean ± SEM as 1.4 ± 0.05 nmol/l for 5 normal Alsatians and as 0.92 nmol/l for 2 Alsatians with hypothyroidism. The individual levels for the 2 affected dogs were 0.7 and 1.2 nmol/l.

FREE THYROXINE INDEX

The results of T4 assay may not correctly indicate the concentration of free physiologically active thyroxine, for example when protein binding is abnormal. Corrections then have to be made. In man, Hamburger (1970) found it valuable to multiply the T4RIA result by the RT3U value to obtain an arbitrary decimal figure which was designated as T7. Visconti (1970) suggested that the T7 value would be useful in the diagnosis of canine thyroid disorders. Rijnberk (1971) noted that the diagnosis of thyroid disease in the dog was hampered by the difficulty in estimating accurately the low level of circulating thyroid hormones. Consequently he considered that calculations of the free thyroxine index (i.e. T7) in an attempt to make corrections for variations in thyroxine binding protein suffered from wide variations due to technical error.

Siegel (1971) considered that the free thyroxine index, the product of T4 assay and RT3U results, allowed a better evaluation of thyroid function than either component alone, as, e.g. if T4 increases and RT3U decreases, the animal may be euthyroid even although the individual values are abnormal as may occur in pregnancy (in women). Thus, if T4 is increased but the binding is also increased the relative amount of free thyroxine available may not be abnormal. Conversely, he stated, if serum T4

is decreased, but relatively all binding sites are saturated (increased RT3U) the animal may be euthyroid.

Kallfelz and Erali (1973) investigated the value of the free thyroxine index (FTI) in the dog, They reported the FTI as a decimal figure by multiplying the T4CPB test result, expressed as micrograms of T4 per 100 ml of serum, by the RT3U result expressed as a decimal. They concluded that since the RT3U test did not seem responsive to changes in thyroid gland status in the dog, the FTI in this species apparently reflected only alterations occurring in the serum T4 concentration. Thus, in the dog at least, the FTI was no more useful than the T4 test alone. Chester, Hightower, Kyzar and Wright (1974) undertook T4 assay and RT3U tests in radiothyroidectomised beagles. They concluded that the T4 and the derived T7 values were useful in confirming clinical hypothyroidism while the RT3U and cholesterol values were not to be relied upon. They indicated that one of the advantages of using T7 figure was that some drugs that affected either the RT3U or the T4 assay affected them both, but in different directions. However, no animals in their tests were given drugs during the experiments. They considered that, in clinical cases especially where animals had been treated with, e.g. the sex steroids or corticosteroids, the T7 figure should be a more accurate way of evaluating

the thyroid function, but they stated that this needed further proof.

Hightower, Kyzar, Chester and Wright (1974) thought that there was some validity in calculating the T7 index because they found that, in their normal dogs at some time during the period of one year of examinations, some had RT3U and/or T4 assay results in the hypothyroid or hypothyroid grey area.

Kelley, Oehme and Hoffman (1974) used a commercial kit to measure T7 (Res-o-Mat ETR diagnostic test, Mallinckrodt Chemical Works, St. Louis). They considered that as a result of their research further evaluation of the test should be conducted in dogs that had abnormal thyroid function. They had used it in normal dogs.

Kelley and Oehme (1974) give some synonyms for the T7 test. It is also known as the thyroxine-resin T3 index (T4/RT3 index), thyroid activity index, corrected thyroid concentration and free thyroxine index. It is calculated as T4(D) x RT3U = T4/RT3 index. T4(D) is also known as T4CPB. They made the tests on sera from normal dogs, horses and cattle but reported little of value.

Capen, Belshaw and Martin (1975) state that there is good correlation between the FTI and measured free T4 values in man but not in the dog. They found that the measurement of free T4 in addition to that of total serum T4 gained nothing for them in diagnosis. So, even if a free T4 value were diagnostically useful in

the dog, the free thyroxine index would still not be a valid substitute.

Kaneko, Baker and Mills (1975) noted that the T3 uptake test and the free thyroxine indices, for example, T7 and FTI, were not as successful in animals in measuring thyroid function as T4 assays or the response of T4 to exogenous TSH administration. Siegel (1977), however, considered that there was excellent correlation between the free thyroxine index and the absolute level of free thyroxine as measured by dialysis, making the FTI a useful measurement of thyroid function. Siegel did not indicate whether he was writing specifically about the dog, and the statement was unsupported by experimental evidence.

Lorenz and Cornelius (1976) and Kallfelz (1977) reiterated the opinion that the FTI was of no more value than T4CPB alone, in the dog. Although the FTI is generally abnormal in dogs with thyroid gland dysfunction this is almost entirely due to changes in T4CPB results and not to alterations in the percentage uptake of T3 by the resin sponge method.

This is as would be expected. The RT3U test has been shown to be of little value in assessing canine thyroid function whereas it has some value in man.

THE USE OF THYROID STIMULATING HORMONE IN DIAGNOSING THYROID STATUS

Introduction

Since the normal function of the thyroid stimulating hormone (TSH) is to increase the amount of T4 and T3 in the circulation, it has been made use of in assessing the function of the thyroid gland when the clinical picture and the results of other thyroid function tests suggest the presence of hypothyroidism. First, blood samples are taken and the hormonal iodine is assayed in one of the usual ways. An injection of TSH is given and at intervals thereafter further blood samples are taken and assayed for PBI, T4 or T3. In euthyroid dogs, the effect of the injection is to increase the circulating levels of thyroid hormone. In dogs with primary hypothyroidism the increase is slight, but in secondary hypothyroidism there is an increase of a variable amount which may almost approach the normal levels.

Response to TSH stimulation has also been assessed by measuring the thyroid uptake of radioactive iodine in vivo.

Thyroid Stimulating Hormone and Protein Bound Iodine

In normal adult dogs, 24 hours after administration of 5 - 10 IU of thyrotropin (TSH) the average increase of plasma PBI was 3.0 mcg/100 ml above the control values, whereas in dogs with primary hypothyroidism, the increase above the control value was seldom more than 0.5 mcg/100 ml and usually it was 1.0 mcg/100 ml or greater in secondary hypothyroidism (Theran & Thornton, 1966: Belshaw, 1967; Siegel & Belshaw, 1968). In one hypothyroid dog, it rose from 1.6 to 1.8 mcg/100 ml (Theran & Thornton, 1966). Quinlan and Michaelson (1967) reported that 15 IU of TSH increased PBI values from 2.6 $\pm$ 0.8 to 5.9 $\pm$ 2.0 mcg/100 ml in normal dogs.

Reid (1968) considered that the ratio of PBI to total iodine was often of diagnostic value but that an accurate differential diagnosis required testing the thyroid response to TSH with subsequent measurement of PBI (or by in vivo ^{131}I uptake tests).

In the opinion of Siegel and Belshaw (1968) and of Mason and Wilkinson (1973), the TSH response test's main use was to distinguish between primary hypothyroidism and hypothyroidism secondary to hypopituitarism. In both disorders, PBI is depressed. In primary hypothyroidism the response to TSH is negligable whereas in secondary hypothyroidism the

response to TSH may approach that in normal dogs following TSH administration. An additional value of the test is that an inadequate response to TSH aids in detecting hypothyroidism in those dogs in which the pre-test PBI values were not clearly depressed below the normal range. Bustad and Fuller (1970) provide the same information. They administered 5 - 10 IU of TSH intramuscularly and compared the PBI level 24 hours later with that immediately before administration of TSH.

Bullock (1970) also reported that estimation of PBI gives a useful index of the response to TSH stimulation. He found that in euthyroid and hypothyroid dogs the mean PBI response 24 hours after TSH administration was 3.1 $\pm$ 1.5 and 0.4 $\pm$ 0.4 mcg/100 ml respectively, a diagnostically significant difference. Bullock considered that 95% of the euthyroid population could be expected to have post-TSH values of 2.2 mcg/100 ml or greater and that 93% of hypothyroid dogs would have values below 2.2 mcg/100 ml.

In normal dogs, the post-TSH value of PBI had more than doubled by 24 hours, whereas in hypothyroid dogs the rise was slight (Lorenz & Cornelius, 1976). Muller and Kirk (1976) stated that PBI normally increased by at least 1.0 mcg/100 ml following TSH administration; a smaller response indicated hypothyroidism. They regard the TSH response test as the

best method for the practitioner to use for diagnosis for, although it is slightly less convenient than a single measurement of serum T4 or T3, it has a diagnostic accuracy of about 95% which is only slightly surpassed by accurate measurements of serum T4 or T3, or by measurements of thyroidal uptake of radioiodine.

Thyroid Stimulating Hormone and T4 and T3

Total thyroxine shows a mean increase of 5.4 mcg/100 ml (range 1.0 - 7.9) at 24 hours post-injection TSH in euthyroid dogs. In primary hypothyroidism no response is seen, whereas in secondary hypothyroidism repeated TSH stimulation may give some response (Siegel, 1971, 1977).

At 8 - 10 hours after intramuscular injection or at 3 - 5 hours after intravenous injection of TSH the maximum response occurred, i.e. a doubling to a trebling of the pre-injection serum T4 values in normal dogs. In thyroidectomised dogs, the administration of thyrotropin did not change the serum T4 concentration. In normal dogs, the tests results had returned to normal or below, 24 hours after TSH ingestion (Kallfelz, 1973).

Hoge, Lund and Blakemore (1974) noted overlapping in serum thyroxine values in clinically normal dogs and in some dogs with signs of hypothyroidism. To distinguish between the 2 groups, one IU of TSH per

3 lb body weight was injected into the lumbar muscle mass. In blood samples collected before and at 1, 4, 8, 12 and 24 hours after the administration of TSH, T4 was assayed by a commercial resin sponge technique. In 19 clinically normal dogs, the mean serum T4 level before TSH administration was 1.6 $\pm$ 0.7 mcg/100ml, range 0.6 - 2.7 mcg/100 ml. Seven of the dogs had T4 values of 1 mcg/100 ml or less. TSH produced a significant increase in T4 within four hours with peak values of 7.4 $\pm$ 1.76 and 7.9 $\pm$ 1.84 mcg/100 ml in the 8 and 12 hours samples, respectively. These mean values were not significantly different. At 24 hours the values were decreasing. The serum T4 levels in four clinically hypothyroid dogs were 0.8, 1.1, 0.8, 1.0 with a mean of 0.9 mcg/100 ml, i.e. as high as or higher than seven of the normal dogs. In only one of these hypothyroid dogs was the 8 or 12 hour sample after TSH stimulation double the pre-stimulation value.

It was recommended previously that the response to TSH be measured at 24 hours after the injection (Kallfelz, 1968; Muller & Kirk, 1969; Bullock, 1970; Bustad & Fuller, 1970; Baker, 1971) but the results of Hoge et al. (1974) indicate that the greatest change in the T4 levels is at 8 and 12 hours and this was also the view adopted by Kallfelz (1973), Belshaw and Rijnberk (1979) and Bush (1979).

Normal dogs have a two to threefold increase in

T4 levels, 10 - 12 hours after TSH injection (Lorenz & Cornelius, 1976; Ihrke, 1979) but in primary hypothyroidism there is little or no response (Lorenz & Cornelius, 1976). In normal dogs the T4 response may be fourfold, in primary hypothyroidism it may be increased but not doubled and patients with secondary hypothyroidism may have varying responses although the increase is not as great as in normal dogs (Kallfelz, 1977).

Lorenz and Cornelius (1976), Kallfelz (1977) and Siegel (1977) considered that the assay of T4 following TSH administration was possibly the most sensitive of the in vitro thyroid function tests available for the dog. It has the disadvantage that the dog has to be kept in hospital for 8 - 10 hours for serial blood sampling (Chastain, 1978).

Belshaw and Rijnberk (1979) measured plasma T4 and T3 responses in 30 normal and 28 hypothyroid dogs. The plasma T4 response to TSH stimulation readily distinguished primary hypothyroidism from other causes of lowered basal T4 and T3 levels. At 8 hours after TSH administration T4 was above 4 mcg/100 ml and below 1 mcg/100 ml in normal dogs and in dogs with primary hypothyroidism respectively. However, the plasma T3 response was much more variable both in time and magnitude in normal dogs. Thus the use of T3 assay, post-TSH, to discriminate between normal and

hypothyroid dogs was less satisfactory. They considered that this reflected individual differences in thyroidal T3/T4 secretion ratios, or in the peripheral conversion of T4 to T3, or in the peripheral disposal of T3.

Sodikoff (1979) has described a method of thyroid function testing in dogs which involves the use of the microdot T4 test by radioimmunoassay. In this, very small quantities of blood are dried on filter paper which is cut into discs of known area and assayed for T4. The TSH stimulation test has been used together with the microdot T4 test. Five units of TSH are given to animals under 20 lbs and 10 units to larger dogs. Blood samples are taken before and four hours later and applied to separate microdot strips which are then analysed as described. Normal animals have doubled T4 levels while hypothyroid animals show no significant changes.

Thyroid Stimulating Hormone and Thyroid Uptake of Radioactive Iodine

Effects similar to those described for PBI and T4 are observed when the in vivo thyroidal uptake of radioactive iodine (RAI) is measured before and after TSH administration to normal dogs and dogs with primary and secondary hypothyroidism (Lombardi, Comar & Kirk, 1962; Quinlan & Michaelson, 1967; Siegel & Belshaw,

1968; Bustad & Fuller, 1970; Kaneko, 1970; Belshaw & Rijnberk, 1979; Bush, 1979). High uptakes of RAI only followed multiple injections of TSH (Lombardi et al., 1962). In normal dogs, the post-TSH increase in RAI was 37% at 24 hours and had reached a maximum of 41% at 96 hours (Quinlan and Michaelson, 1967). Bustad & Fuller (1970) gave 2 IU of TSH twice daily for 3 days, then administered RAI and measured its uptake by the thyroid at 6,24, 72 and 120 hours later. The failure of TSH injections to increase the thyroid uptake of radioiodine indicated primary hypothyroidism. However, a significant increase in the rate and extent of uptake and release suggested a lesion in the pituitary gland and hypopituitarism would be indicated if other diagnostic criteria were met.

Belshaw and Rijnberk (1979) measured thyroidal ^{131}I uptake in cases of spontaneous primary hypothyroidism. The maximum uptake prior to TSH administration was 5.3% of the dose of RAI. After 3 daily doses of 10 IU of TSH the highest value was 6.5% of the dose of RAI.

ASSAY OF THYROID STIMULATING HORMONE

A radioimmunoassay procedure is commercially available for the determination of thyrotropin (thyroid stimulating hormone, TSH) in man in which it is a sensitive indicator of the function of the thyroid gland. When it is combined with a thyrotropin releasing hormone (TRH) response test, it can establish abnormalities in the pituitary or hypothalamic function. In primary hypothyroidism, the levels of TSH in the serum are elevated because T4 is not available to produce the negative feedback which inhibits the release of TSH in the pituitary gland. The test is a very sensitive indicator of primary hypothyroidism in man, as it will pick up elevations in serum TSH levels two or three months before the results of the T4 test are depressed. Kaneko, Baker and Mills (1975), Lorenz and Cornelius (1976), Kallfelz (1977) and Kraft and Gerbig (1977) noted that the TSH assays had not been conducted in the dog but they considered that it should be a useful method for evaluating canine hypothyroidism. The values would be high in primary and low in secondary hypothyroidism. Values for normal dogs would have to be established first.

Chastain (1978) stated that the most sensitive determination of hypothyroidism in man is TSH radioimmunoassay (TSHRIA). He attempted to carry out this

assay in the dog using human thyroid stimulating hormone as his standard. In his research, however, he found that human TSHRIA is not an accurate test of thyroid function in the dog. He considered that TSH assay should provide a sensitive and convenient method for diagnosing hypothyroidism and for distinguishing primary from secondary hypothyroidism, but before this can be done it would be necessary to purify canine TSH in order to carry out a species specific measurement.

IN VIVO TESTS OF THYROID FUNCTION

Two tests involving the administration of radioactive iodine are referred to in this section, the thyroid uptake test and the measurement of protein bound radioactive iodine.

Some of the earliest studies on the uptake of ^{131}I by the canine thyroid gland were carried out by Fredrickson, Ganong and Hume (1955). They found that altered concentrations of dietary iodine affected the uptake.

A detailed account of the clinical applications of the thyroidal ^{131}I uptake test in the dog was given by Kaneko, Tyler, Wind and Cornelius (1959). They interpreted the percentage ^{131}I uptake at 72 hours as follows: 0 - 10% indicated hypothyroidism, 11 - 40% was in the normal range and 41 - 100% indicated hyperthyroidism. The method has also been described by Goyings et al. (1962).

A problem occasionally found in measuring ^{131}I uptake in dogs results from the presence of extrathyroidal radioactivity which may be due to thyroid tissue additional to that which is present in the normally sited gland. This requires the use of special counting equipment shielded from the effects of extrathyroidal radioactivity (Quinlan & Michaelson, 1967).

According to Siegel and Belshaw (1968) most normal adult dogs accumulate between 10 and 30% of the

administered dose of radioiodine within 72 hours. The basenji is an exception. In it maximum uptake of 10% occurs within 15 hours. Impaired uptake of radioactive iodine is consistent with either primary hypothyroidism or deficiency of TSH. Diminished uptake may also be caused by previous exposure to high levels of dietary iodine or iodine in medications. Conversely, abnormally high uptake may be the result of iodine deficiency.

Hightower and Miller (1969) wrote that although the radioactive iodine is usually given intravenously, it may be given orally. There are two ways of reporting the results. The more widely used is the percentage uptake, determined by comparing the concentration of radioactive iodine in the thyroid gland to a previously prepared standard. The other is the neck to thigh ratio in which the concentration in the thyroid gland is compared with that in the thigh region. Care must be taken to exclude the radioactive iodine contained in the urinary bladder. Hightower and Miller summarised the results obtained by others using this test in the dog. They stated that measurement of the urinary excretion of radioactive iodine should be considered together with the thyroidal uptake of radioactive iodine, as the former is also concerned with measuring the thyroid gland's ability to concentrate iodine as iodide. Since nearly all of the administered radioactive iodine is either excreted via the urine or is concentrated by

the thyroid, quantitation of excreted iodine may be considered to assess the reciprocal of uptake. In veterinary medicine, the measurement is very difficult because of the need to collect all of the urine from the patient during the period of the test. Also normal kidney function is an essential feature. Although results were available for man, they had not been reported for animals mainly because of the problem of collecting the total urine output.

The radioactive iodine uptake test is influenced by the renal clearance of iodine (Michaelson, 1969).

When tracer amounts of radioiodine are utilised, no appreciable iodine is added to the system and consequent radiation exposure causes no detectable damage. Generally, the young of a species manifest the highest thyroidal uptake of iodine per gram of thyroid and larger animals usually have larger thyroids permitting larger tracer doses to be used without risk of damaging the thyroid gland (Bustad & Fuller, 1970).

Kaneko (1970) comments that only minimal doses of radioactive iodine should be used as larger doses can cause a functional impairment of the thyroid gland. In the system employed by him, 10 - 30 mcCi are given intravenously to dogs. Ideally the uptake should be measured frequently after injection and a time uptake curve should be constructed for three to four days, but for practical clinical purposes in hypothyroid dogs, a single measurement at 72 hours is usually satisfactory.

However, for the differential diagnosis of hyperthyroidism, the time uptake curve is required. Kaneko recommends deferring the uptake test for at least three weeks if iodine compounds have been administered. He gives an extensive list of substances which affect the ^{131}I uptake. For example, simple iodine-containing materials generally decrease the ^{131}I uptake for a minimum of 10 - 30 days on average and the x-ray contrast media have an effect which may be of 12 months duration, or longer, although the gall bladder media seemed to have a shorter effect. Thyroidal extract, triiodothyronine and ACTH have a depressing effect on uptake for at least two weeks and possibly up to six weeks. He states that diphenylhydantoin and the salicylates have no effect.

Visconti (1970) however, considered that the salicylates did affect the uptake for about a week.

The use of the test by veterinary practitioners was seriously limited because few laboratories were qualified and equipped to perform it. It remained, however, an important corroborative procedure for the additional evaluation of selected patients (Baker, 1971).

Bush (1972a) described the technique which he employed in performing the thyroid uptake test in dogs with ^{131}I. He also used the protein-bound ^{131}I test, collecting blood samples at 24, 48, 72 and 96 hours following the administration of the radioactive iodine.

Kallfelz, Comar and Wentworth (1974), in an extensive review, stated that perhaps the most widely used in vivo veterinary nuclear medical technique was the radioiodine thyroid uptake test.

The in vivo uptake depends considerably on the iodine content of the food. Because most commercial dog foods have such high iodine contents, the uptake values in normal dogs are sometimes as low as those in hypothyroid dogs. Thus it is best to feed a low iodine all (fresh) meat diet for one to two weeks before studying the normal uptake values (Rijnberk, 1974). Rijnberk also discussed the protein bound radioactive iodine test. Radioiodine accumulated by the thyroid gland is incorporated into thyroid hormones. These are secreted into the circulation where they are mainly bound to the proteins as protein-bound radioactive iodine, for example PB^{131}I. This serves as an index of the rate of conversion of thyroid iodide to thyroid hormone. Following administration of a dose of radioactive iodine, blood is taken from the dog and its radioactivity measured after the blood has either been subjected to acid precipitation or has been passed through an ion exchange column to remove inorganic iodide. The value is calculated as a percentage of the administered radioiodine dose per litre of plasma. This test is not useful in the diagnosis of hypothyroidism except in patients with partial destruction of the thyroid in which there is an increased turnover of

iodine and paradoxically, high PB^{131}I values.

There are problems associated with the use of the in vivo thyroid radioactive iodine uptake test, as have already been noted. The test can only be performed at licensed centres, it may require lengthy hospitalisation and it is virtually impossible to standardise the intake of dietary and medicinal iodine in pet dogs (Bush, 1977), although the results generally correlate well with the clinical picture (Bush, 1979).

In human medicine, Evered (1976) considers that ^{131}I tests are rarely required for routine purposes as it discriminates poorly between mild hyperthyroidism, hypothyroidism and the normal state. It has been superseded by other tests.

Because of the problems, Belshaw and Rijnberk (1977) do not regard the test as practical in private veterinary practice. Kallfelz (1977) notes the problem of environmental contamination and states that the procedure has not found wide acceptance in dogs. The administration of radioactive iodine increases the probability of thyroid carcinoma later in life (Siegel, 1977).

EXAMINATION OF BIOPSY SPECIMENS

Introduction

As parts of the diagnostic procedure while the animal is still alive, examination of biopsy samples of thyroid gland or of the skin has been made by a number of workers.

Histological Examination of the Thyroid Gland

This has already been discussed in connection with the aetiology of hypothyroidism.

Histological Examination of the Skin

There is general agreement that the epidermis, in severe cases of hypothyroidism, is atrophied and hyperkeratinised (e.g. Freudiger, 1960, 1962; Goyings, 1961-62; Kral & Schwartzman, 1964; Muller, 1965; Walton, 1965; Mallo, 1966; Thomsett, 1966; Schwartzman, 1966; Muller & Kirk, 1969; Baker, 1971; Capen et al, 1975; Rojko et al., 1978; Martin & Capen, 1979).

While in mild cases the hair follicles look normal with a number in the telogen phase (Walton, 1965), in the more severe cases the follicles generally

are distended and inactive (Muller, 1965; Thomsett, 1966; Rojko et al, 1978; Martin & Capen, 1979). When hair is absent its place in the follicle may be taken by keratinous debris (Goyings, 1961-62; Walton, 1965; Thomsett, 1966; Muller & Kirk, 1969; Belshaw, 1971; Rijnberk, 1971; Capen et al., 1975; Martin & Capen, 1979). Capen et al.(1975) also report the presence of a desiccated secretion in the ears and on the margin of the eyelids. In the "classical" form, inflammation is absent but in some seborrhoeic cases the telogen phase hair follicles have associated acanthosis and a mild mixed inflammatory cell infiltration (Rojko et al., 1978).

The sweat and sebaceous glands associated with hair follicles in telogen are often atrophied (Goyings, 1961-62; Freudiger, 1962; Kral & Schwartzman, 1964; Muller, 1965; Walton, 1965; Muller & Kirk, 1969; Thomsett, 1975).

The dermis is thicker than normal and, in severe cases, shows marked changes due to the collagen and elastin fibres being swollen, disorientated and separated by mucinous fluid (Freudiger, 1960; Goyings, 1961-62; Kral & Schwartzman, 1964; Walton, 1965; Thomsett, 1966, 1975; Bustad & Fuller, 1970; Baker, 1971; Martin & Capen, 1979). There is hypertrophy and hyperplasia of the arrector pili muscles (Goyings, 1961-62; Muller, 1965).

Ojemann (1940), Groth (1962a), Bloom (1959, 1971), Kaneko (1960, 1963, 1970) and Goyings (1961-62) do not consider the lesion to be the counterpart of myxoedema in man but Goldberg and Chaikoff (1952), Lippincott et al. (1957), Freudiger (1960), Kral and Schwartzman (1964), Walton (1965), Thomsett (1966, 1975) and Bustad and Fuller (1970) tend to the view that the mucopolysaccharide material associated with the lesion is, as Baker (1971) puts it, the basis upon which the name myxoedema is applied to the similar condition in man.

Bush (1969a) concluded that it appears that myxoedema or a myxoedema-like condition develops only in severe or prolonged canine hypothyroidism. Rojko et al. (1978) found it in 30% of their cases and, as already indicated, Martin and Capen (1979) have confirmed its presence in severe cases.

These histological changes develop both in spontaneous and induced hypothyroidism. According to Kristensen (1975b) and Kallfelz (1977), apart from the myxoedema, they are not specific for hypothyroidism and are also seen in the skin changes associated with hyperadrenocorticalism and Sertoli cell tumours.

From these reports there can be no doubt that myxoedema is not a frequent occurrence in hypothyroidism in dogs. Furthermore, it is well to note that myxoedema is not a common finding in hypothyrotic humans

either (Evered, 1976). In view of the common picture, (except for the infrequent occurrence of myxoedema in hypothyroidism),it does not appear at present that histological examination of the skin can provide a means of differential diagnosis between a number of dermatoses of endocrine origin.

BLOOD CHOLESTEROL CONCENTRATIONS AND THYROID FUNCTION

Introduction

Cholesterol is the major sterol in mammalian tissues (Cook, 1958). The following introduction is largely based upon the publication of Collins (1975). Body lipids serve mainly as a source of energy for metabolism, have an important function in the make-up of cell membranes and are precursors of the steroid hormones and bile acids. Cholesterol is absorbed into the lymph stream from the gut in both the free and the esterified form. Most of the esters are hydrolysed to the free form, it is thought, before they are absorbed by intestinal cells. Both the blood and the lymphatics convey lipids including cholesterol and it has been noted in man that the normal values vary with age. The levels are lower in younger than in older people.

It is not surprising that cholesterol-free diets are relatively ineffective in lowering the serum cholesterol, for if the diet contains a surplus of protein and carbohydrates these are used as the basic materials in the formation of cholesterol. Although the main seat of the formation of cholesterol is the liver, other tissues and cells of the body also form it and its esters. Most of it is not metabolised as the body is unable to disintegrate the sterol ring.

Cholesterol is the only lipid to be appreciably excreted. Mainly it passes into the digestive tract through the bile, although a small amount is secreted by the mucosa of the gut. Most of this is reabsorbed but part is excreted in the faeces.

The factors that maintain an equilibrium between the intake of cholesterol and its production in the body and its excretion, storage and utilisation include an increase in dietary cholesterol which may lead to a decrease in liver synthesis of cholesterol and an increased excretion via the bile of cholic acid. The fact is that the control of the equilibrium is not well understood for neither the quality nor the quantity of fats in the diet seem to have any effect on the serum lipids except immediately after ingestion.

The plasma lipoproteins are the major components of the globulin fraction of plasma which are responsible for the transport of cholesterol and lipids in the circulation (McCullagh, 1978).

Relationship of Blood Cholesterol Values to Thyroid Function

For over half a century a relationship has been recognised between blood cholesterol concentrations and the state of thyroid function.

Chaikoff, Entemann, Changus and Reichert (1941), Thompson and Long (1941), Glock (1949) and Goldberg and

Chaikoff (1952) noted, in dogs, that serum cholesterol levels varied inverseley with the state of thyroid function following thyroidectomy by surgery or the use of goitrogens. Some dogs developed an increase in serum cholesterol without developing clinical signs (e.g., Binswanger , 1936; Danowski, Man & Winkler, 1946; Glock, 1949). Because of the absence of clinically obvious signs in dogs thyroidectomised, or, at least treated, with propylthiouracil, Mayer (1947) thought that the thyroid function was not needed by dogs under ordinary conditions.

Each of the authors to whom reference will be made agrees that serum cholesterol levels are elevated in varying degree in hypothyroidism even although clinical signs of thyroid deficiency are not apparent.

Rosenman, Byers and Friedman (1952) investigating the hyperthyroid state found an increase in cholesterol metabolism, in that not only is cholesterol synthesis hastened, the rate of excretion and destruction are also accelerated. Conversely, they found there is a reduced rate of cholesterol synthesis in the hypothyroid state and at the same time there is a reduction in the rate of its excretion and destruction. However, these are less than the rate of synthesis and, accordingly, the cholesterol levels in the blood rise in hypothyroidism. Gould, Taylor, Hagerman, Warner and Campbell (1953) demonstrated that the main site of synthesis of cholesterol in the dog is the liver. In cholesterol

fed dogs they found there was a very low rate of cholesterol regeneration and synthesis.

In 1958, Meier and Clark reported that physiologically the thyroid influences the metabolic rate and that there was a significant reverse correlation between the basal metabolism and the cholesterol level. When the basal metabolic rate is low, they said, as in hypothyroidism the cholesterol level is high.

Kaneko (1963) and Michaelson, Quinlan, Casarett and Mason (1967) observed respectively that in naturally occurring and induced hypothyroidism, hypercholesterolaemia developed.

Ekman, Orstadius and Thorell (1968) studied the cholesterol levels in hypothyrotic dogs and found them to be higher in those cases which also exhibited alopecia and adiposity than they were in normal dogs or those with acanthosis nigricans or with dermatosis caused by infections or parasites. Siegel and Belshaw (1968) used knowledge of the cholesterol level as an adjunct in the diagnosis of canine hypothyroidism and noted that, with the exception of hyperadrenocorticalism, few other diseases resulted in the extreme levels of cholesterol that are occasionally seen in hypothyroidism. Although they and Bustad and Fuller (1970) said that only one half to two thirds of hypothyroid dogs have hypercholesterolaemia, its occurrence helps to support a diagnosis, whereas a normal cholesterol value is of no diagnostic significance.

Reid (1969) regarded cholesterol estimations as being unreliable in determining thyroid function in the dog. Kaneko (1970) considered that the diagnostic accuracy of serum cholesterol for hypothyroidism is about 60%. However, when the levels are very high, that is over 500 mg/100ml, and when diabetes mellitus is eliminated, its diagnostic accuracy is greatly increased but other thyroid function tests should also be performed. Jubb and Kennedy (1970) considered that hypercholesterolaemia in dogs is chiefly related to hypothyroidism and thought it was the best chemical index of thyroid activity.

DiScala, Lippe and Segal (1971) found significant differences ($P < 0.001$) in cholesterol levels between normal dogs and dogs with hypothyroidism following thyroidectomy, and considered that these levels were useful in monitoring treatment. All their hypothyroid dogs had serum cholesterol levels elevated 1.5 to 3 times the control value.

Manning, Corwin and Middleton (1973) considered that primary hypothyroidism is the main cause of hyperlipoproteinaemia. Dogs with this condition had significantly lower concentrations of T4 which did not change after the injection of thyrotropin (TSH).

It had been noted by a number of workers that surgical or other forms of thyroidectomy did not always induce hypothyroidism. Capen, Belshaw and Martin (1975) considered that this was because of the presence

of accessory thyroid tissue which readily responded to the prompt increase in endogenous TSH which was secreted in the induced hypothyroid state. Also, they say, there is the possibility that the remaining thyroid tissue undergoes sufficient hyperplasia to sustain additional hormone production. They consider that although the serum cholesterol concentration was an indirect and variable index of thyroid hormone, fasting serum cholesterol concentrations over 300 mg/100ml are often found in spontaneous hypothyroidism. This would include two thirds of the cases in pet dogs. However, hypercholesterolaemia is probably as dependent on diet as upon the severity and duration of the hypothyroidism. Since it occurs in some other canine diseases it cannot be regarded as a specific test for thyroid function. However, levels over 600 mg/100ml are not infrequent in hypothyroidism and this is rare in other diseases.

Thomsett (1975) thought that cholesterol levels were of doubtful diagnostic value in canine hypothyrotic alopecia. Muller and Kirk (1976) also said that it is not specific and, in any case, in one third of hypothyrotic dogs it is of no use in diagnosis as they have normal serum cholesterol concentrations. However, it is a useful measurement for regulating the dose of thyroid hormone in the treatment of cases.

Rogers, Donovan and Kociba (1975) state that, compared with normal dogs, hypothyroid dogs have marked alterations in lipids and lipoprotein levels in the blood. Dogs with a marked

hyperlipidaemia have increased serum concentrations of serum triglyceride, cholesterol and occasionally free glycerol. When the hyperlipidaemia is less marked, only hypercholesterolaemia occurs.

McCullagh (1978) stated that hypercholesterolaemia and hypertriglyceridaemia are often present in the canine blood in disease states. They reflect a variety of secondary hyperlipoproteinaemic states which are associated with the diseases which will be discussed later. The mechanism by which hypothyroidism produces hyperlipoproteinaemia is not certain but it is related to the degradation of low and very low density lipoproteins. When hypercholesterolaemia is excessive, that is over 500 mg/100ml, thyroid dysfunction should always be considered in the differential diagnosis. The hyperlipoproteinaemia usually responds quickly to replacement thyroxine therapy and can be used as an indicator of the correct dosage.

Martin and Capen (1979) noted that the frequent development of hypercholesterolaemia in hypothyroid dogs was the result of the decreased rate of lipid metabolism which was more than counterbalanced by the diminished intestinal excretion of cholesterol and reduced conversion of lipids into bile acids.

Effects of Diseases other than Thyroid Dysfunction on Blood Cholesterol

It is well known that cholesterol levels are affected

by disturbances of health, other than hypothyroidism alone. For example, Lewis, Page and Kolff (1958) showed that after bilateral nephrectomy in dogs, the cholesterol levels were raised. This is also the case in the canine nephrosis syndrome (Hoe & Harvey, 1961; Kaneko, 1970; Buser, 1974; Lorenz & Cornelius, 1976; Muller & Kirk, 1976; McCullagh, 1978). The serum cholesterol levels are also raised in diabetes mellitus (Hoe & Harvey, 1961; Kaneko, 1970; Mason & Wilkinson, 1973; Buser, 1974; Lorenz & Cornelius, 1976; Muller & Kirk, 1976; McCullagh, 1978) and in Cushing's syndrome or hyperadrenocorticalism (Siegel & Belshaw, 1968; Mason & Wilkinson, 1973; Capen et al. 1975; Kelly & Darke, 1976; Lorenz & Cornelius, 1976; Muller & Kirk, 1976; McCullagh, 1978). This is in accordance with the knowledge that the adrenal gland makes a significant contribution to the regulation of plasma lipid metabolism (Power & Luzio, 1958). They are raised in pancreatitis and (obstructive) hepatosis (Kaneko, 1963; Lorenz & Cornelius, 1976; McCullagh, 1978) and pyometritis (Hoe & Harvey, 1961; Buser, 1974). In these various disease conditions, there is a moderate elevation of the serum cholesterol levels (Muller & Kirk, 1976). This is not always so, and Orstadius (1971) found that in 18 dogs with liver insufficiency only one had a value of 500 mg/ 100 ml and he considered the others to be within the normal range.

On the other hand, Hoe & Harvey (1961) found that dogs suffering from viral diseases had low values, e.g. 50 mg/100 ml, as the result of debility.

Bush (1980) summarises the situation by stating that with reduced liver function the cholesterol levels may fall. However with the secondary liver disease which is associated with diabetes mellitus, hyperadrenocorticalism, hypothyroidism and the nephrotic syndrome, the cholesterol levels are often increased. Increased cholesterol levels are often found in extrahepatic cholestasis.

Relationship of Blood Cholesterol to Diet

A number of workers, of whom Grigaut and L'Huillier (1912) were amongst the earliest, have discussed the effect of a canine diet rich in fat or with added cholesterol. Steiner and Domanski (1941) were unable to produce even a moderate hypercholesterolaemia in dogs on a cholesterol rich diet. It seemed that it might be necessary to feed a protein deficient diet with high fat and cholesterol content before hypercholesterolaemia occurred (Li & Freeman, 1946). According to Steiner and Kendall (1946), cholesterol feeding only caused hypercholesterolaemia if the dogs were previously made hypothyroid. Mann and Stare (1954) considered that increased absorption of dietary cholesterol did not necessarily increase the blood cholesterol levels. However, a mild hypercholesterolaemia was induced in

10 mongrel dogs fed a purified diet to which cholesterol was added but, despite the constant cholesterol intake, there was a great individual variation in the cholesterol level from week to week in the dogs (Shull, Mann, Andrus & Stare, 1954). This led to the view, expressed by Meier and Clark (1958) that hypercholesterolaemia could result simply from increased food intake, especially in obese animals with their relatively greater food requirements. In a few obese animals they noted that cholesterol levels were normal and they ascribed this to the possibility that these animals had a temporarily increased basal metabolism due to a larger surface area.

Hoe & Harvey (1961) estimated the total serum cholesterol and cholesterol ester values for two groups of normal dogs. The first group consisted of clinically normal kennel dogs of varying ages, kept and fed alike. The other group, also of various ages, consisted of domestic pets on very varied diets which generally contained a proportion of household scraps. Age had little effect on cholesterol values. The household pets had higher cholesterol values than the kennel kept dogs and it was assumed that the diet of the domestic pets was considerably higher in cholesterol because it contained items normally eaten by people. They also found raised levels in two cases of hypothyroidism. Kaneko (1963) and Michaelson et al. (1967) considered that the serum cholesterol levels fluctuated with the

diet, as well as being elevated in hypothyroidism.

Schiller, Berglund, Terry, Reichlin, Trueheart and Cox (1964) investigated the cholesterol levels in a large number of pet dogs and in laboratory kept dogs. The pet dogs' diet included the sort of food that people eat. Like Hoe and Harvey (1961) they found that the level of serum cholesterol in the pet dogs was higher than in laboratory kept ones. They considered that this was the result of the pet dogs eating a diet partly like a human one. Schiller et al. (1964) noted that high values occurred in a number of young growing animals. The point, of course, is that as Michaelson (1969) has indicated, if dietary content affects the cholesterol levels, this may affect the diagnostic accuracy of cholesterol estimation in hypothyroidism. Even in normal dogs, when a diet high in fat is fed, the serum cholesterol levels tend to range widely (Doxey, 1971).

It was for this reason that Munson and Belshaw (1966-67) had previously made the recommendation, repeated later by others such as Mason and Wilkinson (1973), that serum cholesterol estimations should not be performed until after a fasting period of 12 - 18 hours.

High fat diet (Mason & Wilkinson, 1973; Buser, 1974), especially if the fat is saturated (Muller & Kirk, 1976) is associated with hypercholesterolaemia of, at least, moderately elevated level. Both the nature of the diet and the time of feeding influence

the cholesterol level (Lorenz & Cornelius, 1976).

Kronfeld, Johnson and Dunlap (1979) found that in racing huskies, there was an inherited predisposition in some dogs to hypercholesterolaemia induced by diet. They found that this hyper-responsiveness to diet was unrelated to sex or age and that the findings were consistent with the inheritance of a single autosomal dominant gene. They were unable to identify the specific dietary factors that were necessary for the expression of the hyper-responsive trait. However, it seemed likely that dietary fat was important. These dogs showed no signs of hypothyroidism, diabetes mellitus or any other disorder and they raced successfully.

Other Factors affecting Cholesterol Concentrations

Boyd and Oliver (1958), reviewing the literature at that time, considered that it was unlikely that prolonged administration of physiological doses of epinephrine would influence the plasma cholesterol levels. Heparin in high dosage lowers but in small dosages had no significant effect on the concentration of cholesterol. Aspirin, nicotinic acid, the inhalation of oxygen, irradiation by ultra-violet light and a variety of other substances and procedures are said to lower the plasma cholesterol levels but this is neither a consistent nor a marked action. In their review they also note that both thyroxine and triiodo-thyronine depress the level of circulating cholesterol

in hypothyroid and euthyroid people.

Lewis et al. (1958) noted that the changes in serum cholesterol and lipoprotein concentration were depressed after the administration of steroid hormones, or when increased adrenal size and activity were present. Adrenalectomised dogs maintained on desoxycorticosterone acetate (DCA) have a progressive increase in plasma phospholipids and cholesterol. If the DCA is withdrawn and cortisone is substituted, the levels are rapidly restored and maintained at an elevated rate. It thus seems that the regulation of lipid metabolism can be affected through the action of cortisone. When dogs with high levels of blood cholesterol are treated with dinitrophenol (DNP), the cholesterol level declines to almost normal (Hollander, Thompson, Barrett & Berlin, 1967). DNP is used in the treatment of dogs for internal helminth parasites.

Bush (1970b) found that the administration of triiodothyronine (T3) or the feeding of iodine to euthyroid dogs did not produce any abnormal change in cholesterol levels. Collins (1975) noted that oestrogen decreased the half-life of plasma cholesterol whereas ovariectomy increased it. Of course, the most consistent way of reducing hypocholesterolaemia due to hypothyroidism is to institute appropriate thyroid therapy as Hollander et al. (1967), Kaneko (1970) and many others have shown.

Hypothyroidism, Hypercholesterolaemia and Atherosclerosis

Belshaw (1971) states that the hypercholesterolaemia that occurs in one half to two thirds of dogs with hypothyroidism is sometimes accompanied by medial atherosclerosis of the coronary arteries and of some vessels in the kidney, spleen, thyroid, adrenals and elsewhere.

Mahley, Weisgraber and Fry (1973) demonstrated that hypothyroid dogs fed cholesterol developed hypercholesterolaemia, but only certain of those dogs went on to develop atherosclerosis. Mahley, Weisgraber and Innerarity (1974) fed high cholesterol diets to dogs with induced hypothyroidism and found that the hyperlipoproteinaemia induced by this treatment could give rise to atherosclerosis. Some dogs, however, were referred to by them as hypo-responders and in these dogs, although the plasma cholesterol levels were from 2 to 5 times the normal or up to 750 mg/100ml, significant atherosclerosis did not develop. The dogs they refer to as hyper-responsive developed significant and often complicated atherosclerosis. They had plasma cholesterol levels in excess of 750 mg/100ml and most of the increased cholesterol was present in lipoproteins with a density of less than 1.006 gm/ml.

The atherosclerosis which may occur in dogs with severe hypothyroidism and longstanding hyperlipidaemia may result in myocardial haemorrhage and ischaemic necrosis (Martin & Capen, 1979).

Manning et al. (1973) made some interesting observations on familial hyperlipoproteinaemia and thyroid dysfunction in beagles. They found that certain strains of beagles had a familial hyperlipoproteinaemia and they concluded that the major cause of this was a primary hypothyroidism in these dogs as they had significantly lower concentrations of T4 but essentially no change in the levels of serum T4 after ingestion of thyrotropin. Also these dogs had a relatively low in vitro T3 uptake test result. McCullagh (1978) considered that the incidence of familial hyperlipoproteinaemia of thyroid origin in the dog might be higher than the single report by Manning et al. (1973) suggested. Manning (1979) referring to the earlier publication (Manning et al., 1973) recalled the familial nature of the disease and stated that it was probably hereditary. The three distinguishing characteristics of familial hypothyroidism in the beagles he examined, were profound hypothyroidism, marked persistent hyperlipoproteinaemia and progressive alterations of various kinds in the morphology of the thyroid gland. It would appear that this is a different syndrome from that described by Kronfeld et al (1979) as the inherited predisposition to hypercholesterolaemia. The latter observed in huskies was not associated with hypothyroidism. Crispin and Barnett (1978) were able to trace relatives of only 1 of their 5 cases and found that her mother and daughter were also hyperlipoproteinaemic, the daughter showed signs of hypothyroidism, indicating that the hyperlipoproteinaemia and the hypothyroidism

with which it is associated may have a hereditary basis in the Alsatian breed.

Levels of Plasma or Serum Cholesterol Reported in the Literature

Generally the lower end of the normal range, i.e. in euthyroid dogs, is considered to be about 90 - 125 mg/100 ml. The upper end of the normal range has been reported as 150 mg/100 ml by Kallfelz (1973) and about 200 mg/100 ml by Lewis et al. (1958), Quinlan and Michaelson (1967), Michaelson (1969) and Bush (1972b). Those who have reported it to be about 250 mg/100 ml are Meier and Clark (1958), Cline and Berlin (1963), Kaneko (1963), Mallo (1966) and Hightower, Kyzar, Chester and Wright (1974). An upper level of 280 mg/100 ml in the normal range has been reported by Lombardi, Comar and Kirk (1962), Mallo and Harris (1967) and Muller and Kirk (1976). An upper level of 300 mg/100 ml has been reported by Schwartzman (1966), Munson and Belshaw (1966-67), Hollander, Thompson, Barrett and Berlin (1967), Baker (1971) and Mason and Wilkinson (1973). Sometimes higher levels have been reported as the top of the normal range. For example, Ekman et al. (1968), Wilson, Dickson and Frost (1961) and Mallo and Harris (1967) give 416 mg/100 ml, 430 mg/100 ml and 480 mg/100 ml, respectively.

Two groups of workers studying normal dogs were able to compare dogs kept in kennels and fed a regular

type of dog diet with dogs which were kept as household pets and which received a variety of foods, including scraps. Hoe and Harvey (1961) report that the range for the kennelled dogs was 110 - 286 mg/100 ml and for the household pets 110 - 470 mg/100 ml. Schiller et al. (1964) reported for their kennelled group a range of 56 - 260 mg/100 ml and for their household animals 90 - 973 mg/100 ml, with means of 133 and 225 respectively.

A number of workers, some already cited, have quoted average or mean figures for blood cholesterol levels in normal dogs. Starting with the lowest levels given, these are 121.5 mg/100 ml (Rajan & Mohiyuddeen, 1973), 127 ± 34 SD (Quinlan & Michaelson, 1967), 146 ± 5.1 (Kallfelz, 1968), 153 ± 32.8 (Bush, 1972b), 159 ± 32 (Chester, Hightower, Kyzar & Wright, 1974), 172 ± 34 (Michaelson, 1969), 180 (Muller & Kirk, 1976), 197 ± 42 (DiScala et al., 1971), 200 (Cline & Berlin, 1963), 200 ± 50 (Buser, 1974), 201 ± 59 (Hollander et al., 1967), 214 (Mallo & Harris, 1967), 238 ± 6 (Ekman et al., 1968) and 258 ± 36.3 (Hoe & Harvey, 1961).

Boyd and Oliver (1958) gave figures of 140 and 180 for dogs on low and high fat diets respectively. Rogers et al. (1975) give a figure of 149 ± 5.6 for kennelled dogs.

Reports on the levels found in cases of canine hypothyroidism are numerous. Again the pattern followed in quoting them here is of going from the lowest to the

highest levels reported. They are 99 - 2800 mg/100 ml (Rogers et al. 1975), 125 - 814 (Thomsett, 1975), 135 - 220 (Kaneko, Tyler, Wind & Cornelius, 1959), 250 - 800 (Moser, 1966), 260 - 1,454 (Schalm, 1975), 300 - 800 (Meier & Clark, 1958), 333 - 530 (Mallo, 1966), 336 - 535 (Hightower, Muller & Kyzar, 1969), 380 (Theran & Thornton, 1966), 580 - 700 (Hoe & Harvey, 1961) and 590 - 600 mg/100 ml (Bryan, 1960). Rogers et al. (1975) give a mean of 193.5 $\pm$ 17.5 SD and Michaelson (1969) gives a figure of 267 $\pm$ 26 SD as the level encountered in cases of hypothyroidism. Munson and Belshaw (1966-67) considered that levels of over 275 mg/100 ml were indicative of hypothyroidism. Bush (1970a, 1972a and 1977) has quoted figures of more than 350 and more than 400 and Schwartzman (1966) considers that levels of over 500 are indicative of hypothyroidism. These workers and others have all commented that a high level of cholesterol alone is insufficient upon which to base a diagnosis and that other direct evidence of hypothyroidism should also be obtained.

Levels of cholesterol have also been published in respect of dogs that had been subjected to thyroidectomy, either by chemical, including radio-active iodine, methods or by surgical removal of the gland. Levels reported include 118 - 141 mg/100 ml (Rajan & Mohiyuddeen, 1973), 128 - 256 (179 $\pm$ 36.7 SD) (Bush, 1972b), 200 - 440 (DiScala et al., 1971), 226 $\pm$ 66 SD

(Chester, Hightower, Kyzar & Wright, 1974), 274 - 1,000 (Cline & Berlin, 1963), over 300 (Paul, Donohue & Holmes, 1975), 317 - 371 (Orstadius, 1971) and 410 - 1,160, mean 726 (Hollander et al., 1967).

Although a number of workers have regarded cholesterol estimation as being of little value in diagnosing hypothyroidism, a considerable number of those cited have stated that it is of particular value in supporting a diagnosis when the levels are high and when clinical and other laboratory findings are also indicative of hypothyroidism. A number of the authors consider that since hypercholesterolaemia resulting from hypothyroidism responds to treatment for hypothyroidism, the alteration in level following treatment helps to indicate the value of the treatment, that is it acts as a monitor of therapy. For example, Mallo (1966) gave figures for two cases before and after treatment. The pre-treatment level in one case was 530 mg of cholesterol per 100 ml and two and four weeks following treatment the levels were 175 and 234 mg/100 ml respectively. In the other case, the level before treatment was 333 mg/100 ml and three weeks later it was 170 mg/100 ml.

One of the more interesting and detailed studies of serum cholesterol levels in the dog was conducted by Ekman et al (1968). In a total of 108 dogs, they found the following: 48 normal dogs had a range of from 144 - 416 mg/100 ml, mean 238 $\pm$ 60; in 17 dogs of normal plumpness which also had alopecia, the range was 234 - 581 mg/100 ml, mean 255 $\pm$ 43.1 in two adipose dogs which

also had alopecia the range was 357 - 424 mg/100 ml, mean 391; in 11 dogs with adiposity but normal skin, the range was 221 - 393 mg/100 ml, mean 319 ± 67; in 15 cases of acanthosis nigricans, the range was 161 - 315 mg/100 ml, mean 235 ± 145; in 15 cases of dermatosis, the range was 105 - 231 mg/100 ml, mean 218 ± 63.

Kallfelz (1977) noted that values, after 12 hours of fasting, of above 125 - 250 mg/100 ml, which are generally regarded as being within the normal range, may be indicative of hypothyroidism if supported by the clinical findings and the results of other thyroid tests.

So far, in this review, the blood cholesterol concentrations quoted have been as given by the original authors, and thus, for even very recent publications, have not been given as units in the Systeme Internationale (SI units). Crispin and Barnett (1978) reported mean ± SEM serum cholesterol values in 5 hypothyroid Alsatian dogs, in SI units, as 15.6 ± 0.692 mmol/l, the range being 13.4 to 17.8 mmol/l. (In the older system these are 603.72 ± 26.80 mg/100 ml and 518.60 to 608.90 mg/100 ml). In 10 normal Alsatians the mean ± SEM serum cholesterol was 4.84 ± 0.273 mmol/l, which equates to 187.31 ± 10.60 mg/100 ml. The difference in serum cholesterol concentration between the two groups of dogs is highly significant ($P < 0.001$).

HYPOTHYROIDISM AND ANAEMIA

Introduction

In human medicine, it has been recognised for many years that there is an association between anaemia and hypothyroidism and this has been reviewed by Cline and Berlin (1963). The three types of anaemia, in man, associated with hypothyroidism are:

a) a normocytic anaemia responsive to thyroxine alone,

b) a hypochromic anaemia responsive to iron therapy alone,

c) pernicious anaemia corrected by vitamin B_{12} alone.

The haematology of canine hypothyroidism has been reported or discussed by many workers.

Freudiger (1960) refers to the occurrence of secondary anaemia. Cline and Berlin (1963) described it in the dog as of the depression type i.e. a dyshaemopoietic anaemia, in which the rate of erythropoiesis was strikingly diminished after thyroid gland ablation but in which the survival rate or life span of the red blood cells (RBC) was found to be normal. They found a reduction of 38% in total RBC volume and a reduction of 19% in the plasma volume in their thyrectomised dogs. Hollander, Thompson, Barrett and Berlin (1967) also reported a reduced total RBC volume.

The anaemia sometimes associated with canine hypothyroidism is moderate, normochromic and normocytic (Kaneko, 1960, 1963, 1970). The stained smear, he states, shows little or no evidence of active erythrogenesis such as anisocytosis, polychromasia or nucleated red cells and it is characteristic of the depression anaemia associated with, e.g. neoplasms and chronic infections. Leptocytes may be especially prominent.

Schalm (1965), Mallo (1966) and Bustad and Fuller (1970) also refer to the anaemia, the first describing it as borderline. It is rarely manifested clinically, but is often noted subclinically on laboratory examination (Munson & Belshaw, 1966-67; Theran & Thornton, 1966; Bush, 1969a; Belshaw, 1971; Rijnberk, 1974).

Others agree that it is a mild normocytic, normochromic anaemia with a decreased rate of RBC formation, manifested rather consistently in canine experimental hypothyroidism (Hollander et al., 1967; Baker, 1971) and in most spontaneously occurring cases (Kaneko, 1970; Capen, Belshaw & Martin, 1975; Kallfelz, 1977; Martin & Capen, 1979). Bush (1970a) observed it in 40% of his series of hypothyroid dogs. He comments that, in most cases, there appears to be little active erythrogenesis; leptocytosis may be prominent and hypochromasia may sometimes be seen. He regards it as non-specific supporting evidence of the disease (Bush, 1972a, 1977). Doxey (1971) remarks that, because of the variable degree of the anaemia, the results of

haematological investigations are diagnostically useful only when considered in the light of the clinical and other laboratory findings. However, as Kaneko (1970) and Kallfelz (1977) observe, when an unexplained moderate, normochromic, normocytic anaemia of hypoplastic or depression type, unresponsive to the usual therapeutic measures, is encountered, the possibility of hypothyroidism should be included in the differential diagnosis.

Schalm (1975) reported slight to moderate anaemia in 7 cases and borderline anaemia in one case, in 11 hypothyroid dogs. Reporting the extremes were Bryan (1960) who found marked anaemia in the one case he reported, and Kristensen (1975b) who observed no abnormalities in erythrocyte sedimentation rate, haemoglobin, haematocrit and RBC and white cell counts in his six cases of thyroxine-responsive alopecia.

From their reviews of the literature on the disease in man, Cline and Berlin (1963) and Hollander et al. (1967) suggest that the anaemia, i.e. the reduction in the rate of RBC synthesis and the reduced total circulating RBC volume, is the result of reduced oxygen demand by the body, reflecting the lower metabolic rate of hypothyroid patients. The additional and alternative theory referred to, is that thyroxine acts directly in erythropoiesis by some, as yet unknown, non-calorigenic process. Hollander et al. (1967) were of the opinion that there could be a dissociation

between metabolic rate and erythropoiesis and that thyroxine might act by some pathway other than by increasing 0_2 consumption. Lewis (1977) regards the anaemia of hypothyroidism (and hypopituitarism) as being a shrinkage of the oxygen delivery mechanism, that is, a response to the need for less 0_2 because of the reduced metabolic rate.

Although the complete nature of the aetiology of the anaemia has still to be resolved, it is fully accepted that it is strongly related to the thyroxine levels in the body as it can only be rectified by restoring euthyroidism through the administration of thyroxine (Cline & Berlin, 1963; Munson & Belshaw, 1966-67; Hollander et al., 1967; Baker, 1971; Belshaw, 1971; Capen et al., 1975). Cline and Berlin (1963) observed no increase in erythrogenesis following the administration of iron or vitamin B_{12} nor did Hollander et al. (1967) who also treated their cases unsuccessfully with dinitrophenol, copper, cobalt, pyroxidine and folic acid.

The following provides a more detailed account of the anaemia reported in the literature.

Red Blood Cells (RBC)

The RBC count is reduced (Freudiger, 1960). In his single case, Bryan (1960) recorded 4.37 million RBC/mm^3. Cline and Berlin (1963) thyroidectomised

7 previously normal dogs with the particular intention of studying the effect of induced hypothyroidism on the haemogram. They reported the following "before" and "after" thyroidectomy counts of RBC and reticulocyte percentages in the peripheral blood.

Normal Dogs (n = 7)		Thyroidectomised Dogs	
RBC	Reticulocytes	RBC	Reticulocytes
$10^6/mm^3$	%	$10^6/mm^3$	%
-	0.26	5.38	0.21
7.35	0.40	5.75	0.27
7.85	0.40	5.47	0.38
8.43	0.31	6.05	0.35
8.11	0.20	7.19	0.10
6.58	-	-	-
6.98	0.21	6.36	0.25

They note that the RBC count had declined to about three-quarters of pre-ablation level, after at least a year.

In their one case, Theran and Thornton (1966) did not observe nucleated RBC. Hollander et al. (1967) reported the counts in 16 dogs before and after thyroidectomy. In the normal dogs, the counts were 7.44 ± 0.72 million RBC/mm^3 and reticulocytes were 0.32 ± 0.26% (mean $\pm$ SD). The comparable figures, post-ablation, were 5.81 ± 0.38 million RBC/mm^3 and reticulocytes were 0.29 ± 0.22%. The difference

between the reticulocyte percentages was not significant but the P value (t test) between the means of RBC counts (and haematocrit and haemoglobin) was at least 0.01.

Hightower et al. (1969) stated that the RBC count was low or "lowish normal" in an Irish setter with hypothyroidism. Nucleated erythrocytes may appear in the circulation (Belshaw, 1971; Capen et al., 1975).

Schalm (1975) reported the following values for 11 dogs with hypothyroidism: 4.08, 6.0, 5.7, 4.6, 5.2, 5.0, 4.2, 4.6, 5.2, 6.1 and 3.2 million RBC/mm^3; reticulocyte numbers were low and leptocytes may be prominent, their presence in large numbers possibly causing the diphasic ESR he recorded in one of his cases.

The decline in RBC numbers is also found in hypopituitarism (Lewis, 1977).

The normal value in adult dogs, of various breeds and ages and of both sexes, for RBC is 5.5 to 8.5 (6.4) millions per mm^3, and reticulocytes are 0 - 0.5% (Doxey, 1971).

Erythrocyte Sedimentation Rate (ESR)

In hypothyroid - hypercholesterolaemic dogs the sedimentation rate is usually accelerated (Meier & Clark, 1958). It is increased in canine hypothyroidism (Freudiger, 1960, 1962; Bush, 1970a; Rijnberk, 1971, 1974; Belshaw & Rijnberk, 1977). In one case Bryan (1960) recorded 36mm/30 minutes and in another case Hoffer (1962) recorded ESRs of 35mm/30 minutes

and 51mm/hour. Schalm (1965, 1975) found it to be significantly increased in 7 of 11 cases and he remarks that alterations in the skin from any cause, including hypothyroidism and Cushing's syndrome, may be associated with an elevated ESR in dogs. He observes that the ESR could be influenced by the changes occurring in the blood vessel walls in hypothyroidism described by Clark and Meier (1958).

From the mean ESR $\pm$ 2 SD of the dogs he studied, Bush (1970a) considered that a rate of 7 mm/hour, or more, was significant and above 10 mm/hour very significant. Eight of 10 dogs in a series had elevated ESR, six in excess of 15 mm/hour and three of those had values over 70 mm/hour. Of 40 hypothyroid dogs, about two-thirds showed an increased ESR and/or hypercholesterolaemia (Bush, 1977). He (Bush, 1970a) considered that the raised ESR is due to abnormal levels of serum proteins and that the increase in cholesterol has little effect on the ESR. He cites Jasper and Jain (1965) who were unable to find any connection between lipaemia and the ESR in dogs.

In considering diagnosis, Bush (1970a) indicated that increased ESR, elevated cholesterol levels and normocytic, normochromic anaemia provide strong evidence of hypothyroidism when the patients show clinical signs characteristic of the disease. He, like others, recognises that the ESR and cholesterol changes are not specific for hypothyroidism as they can also

be affected by other pathological processes, especially liver damage. However, he notes that the majority of non-hypothyroid dogs with liver damage did not show a marked elevation of either ESR or cholesterol.

The normal ESR for adult dogs is less than 1 mm/ hour (Doxey, 1971).

Packed Cell Volume (PCV: Haematocrit)

In single cases of hypothyroidism, the following PCVs were reported, 27 - 30% (Bryan, 1960), 29% (Hoffer, 1962) and 31% (Theran & Thornton, 1966). Cline and Berlin (1963) reported that the anaemia developed slowly and that a consistent decrease in the haematocrit was not detectable until nearly a year after thyroidectomy, the PCV showing a decrease of 18 - 35% of the control values. In the normal controls the mean was 50% (range 44.5 - 55.8%) and after thyroidectomy it was 38% (range 36.1 - 43.2%).

Before thyroid ablation, in 16 normal dogs the PCV was 50.3% $\pm$ 4.48 and afterwards it was 38.7% $\pm$ 3.42 (Hollander et al., 1967). The reduction from the former value was about 23%, a significant reduction, they state. The change occurred some six months after thyroidectomy and three months after the onset of hypothyroidism.

Others reporting decreased PCV include Munson and Belshaw (1966-67), Belshaw (1971), Capen et al. (1975) and Lewis (1977)

Schalm (1975) reported the PCV of 11 hypothyroid dogs as 27, 37, 31, 30, 40, 30, 32, 35, 41, 41 and 24% respectively. He considered that the haemogram showed slight to modest anaemia (PCV < 36%) in 7 dogs and borderline anaemia (PCV 37%) in one dog. Dogs with PCV of less than 37% are in a state of anaemia, states Hathaway (1974) who found in 75 cases of non-regenerative anaemia that 4 were hypothyroid. A PCV of < 36% is supporting evidence for the diagnosis of hypothyroidism (Bush, 1975).

The PCV in normal adult dogs is 37 - 55% (45%) according to Doxey (1971).

Haemoglobin Concentration

The following haemoglobin concentrations have been reported in cases of canine hypothyroidism.

Haemoglobin g/100ml	Author
10.8	Meier and Clark (1958)
8.5 (1 case)	Bryan (1960)
12	Rijnberk (1971, 1974) Belshaw & Rijnberk (1977)

Cline and Berlin (1963) recorded a mean of 17.6g/100 ml (range 15.7 - 19.3g/100 ml) in their 7 normal dogs and, post-ablation, of 13.3g/100 ml (range 12.2 - 14.8g/100 ml).

Hollander et al. (1967) in their 16 cases, recorded

the haemoglobin concentration as 17.4 ± 1.30g/100 ml before thyroidectomy and as 13.3 ± 0.98 g/100 ml afterwards. Schalm (1975) in 11 hypothyroid dogs, recorded 8.5, 12.5, 10.2, 9.8, 13.3, 10.0, 10.2, 11.8, 13.5, 15.0 and 8.8 g/% (mean 12.9, range 8.8 - 15.0 g%). Lewis (1977) also referred to a fall in the haemoglobin level.

The normal haemoglobin level for dogs is 12 - 18g/100 ml (Doxey, 1971). Ekman (1976) points out that when animals are excited the level may be considerably raised.

White Blood Cells (WBC)

The white cell count is normal or slightly raised with a moderate lymphopenia and a neutrophilia, in canine hypothyroidism (Freudiger, 1962). In one case (Bryan, 1960) the total white cell count was 13,000 per mm^3 with a normal differential count of segmented forms (60%), lymphocytes (32%) and eosinophils (6%). There may be a leucocytosis (Kaneko, 1960). However, the differential leucocyte count is usually normal, a feature that helps to distinguish hypothyroidism from Cushing's syndrome (Schalm, 1965).

In his cases, Bush (1970a) reported that the total and differential WBC counts did not reveal any consistent abnormality, although 2 cases of acanthosis nigricans had a marked eosinophilia. Another of his cases,

a dog with secondary hypothyroidism (diagnosed on the basis of the TSH stimulation test), had a marked leucopenia.

The leucocyte count varied from low normal (8,300) to a moderate leucocytosis (36,500) in 11 dogs (Schalm, 1975). Only one of his cases, he states, exhibited stress typical of increased secretion of adrenal glucocorticoids. He suggested that one might expect a leucocyte pattern opposite to the stress reaction as a result of the decreased metabolic rate, as was the situation in 6 of his 11 cases. The findings in 3 dogs, of a leucocytosis due to neutrophilia with a shift to the left, increased monocyte numbers, normal or high lymphocyte numbers and a normal or increased number of eosinophils, were suggestive to him of changes in the devitalised skin due to infection.

Normal leucocyte values, expressed as numbers per mm^3, are total WBC 6,000 - 11,500 (10,100), neutrophils mature 3,600 - 11,500 (6,300) or 62%, neutrophils immature 0 - 450 (70) or 0.5%, lymphocytes 720 - 4,800 (2,500) or 25%, monocytes 180 - 1,500 (530) or 5.5%, eosinophils 120 - 1,500 (700) or 7% (Doxey, 1971).

MATERIALS AND METHODS

MATERIALS AND METHODS

DOGS

During the three-year period which covered the beginning of this study, the following numbers of dogs attended the Small Animal Clinic of the Royal (Dick) School of Veterinary Studies, for all purposes associated with an outpatient clinic.

Year	Male	Male neutered	Female	Female neutered	Total
1976	1724	24	1453	113	3314
1977	1604	23	1190	126	2943
1978	871	7	611	56	1545
Total	4199	54	3254	295	7802

There is no reliable knowledge about the numbers, breeds or breed types, age and sex distribution of the local dog population. Those entering the Clinic may or may not be in proportion to the local population. However, the Clinic is very long-established, has both a regular and sporadic clientele, provides a well-recognised service to the community, has the supporting resources of surgical and medical in-patient wards conducted by the appropriate Departments of the School, and has access to laboratory and other aids to diagnosis. It is run on a fee-paying basis similar that that of local private practices. Thus, even if the Clinic's case load is not proportionately representative of the local canine population, it is representative of cases seen by private practitioners in the area. In

addition, however, cases are also referred by private practitioners. Such cases, when medical in nature, are usually submitted because of difficulty in diagnosis and this may, to a slight extent, affect the representative nature of the cases which are about to be discussed.

From this case load, including dogs referred as in-patients to the Department of Veterinary Medicine, cases were selected, on the basis to be described, to form three groups, namely dogs with suspected hypothyroidism, other suspected hormonal diseases and non-hormonal diseases with skin lesions. This last group was further sub-divided into cases of pyoderma, allergic skin disorders and external parasitism. A fourth group of normal dogs was also examined. When the selection had been completed, the groups consisted of the numbers shown in Table 1.

Table 1.
Numbers of dogs in each group investigated.

Classification	Group	M	Mn	F	Fn	Total	Percentage
Normal dogs	N	36	2	28	2	68	18.53
Hypothyroid suspected	HS	14	1	29	3	47	12.80
Other hormonal	OH	21	4	18	4	47	12.80
Non-hormonal	NH						
a) Pyoderma	P	59	1	35	4	99	27.00
b) Allergic	A	22	3	23	9	57	15.50
c) Ectoparasitic	EP	25	0	22	2	49	13.40
Total		177	11	155	24	367	

M: male Mn: male neutered F: female Fn: female neutered

Table 2 sets out the abbreviations used in some of the tables for the breeds of dogs. When the description, terrier, is used, this implies a small terrier type dog not of pure breeding. The term terrier X implies a small dog of nondescript cross breeding. The suffix X to other breed names indicates that the dog is a mongrel with the named breed predominant.

Table 2

Abbreviations used in the thesis for breeds of dogs

Airedale	Air.	Lakeland Terrier	Lake T.
Alsatian	Als.	Lurcher	Lur.
Beagle	Bea.	Old English Sheepdog	O.E.S.
Bearded Collie	Beard. Col.	Pekinese	Pek.
Border Collie	B. Col.	Pointer	Poi.
Border Terrier	B. Ter.	Poodle	Poo.
Boxer	Box	Pyrenean Mountain Dog	P.M.D.
Cairn Terrier	Cai.	Rough Collie	R. Col.
Chow Chow	Chow	Scottish Terrier	Scot. T.
Collie	Col.	Shetland Collie	Shet. C.
Dachshund	Dac.	Short Haired Fox Terrier	S.H.F.T.
English Setter	E. Set.	Springer Spaniel	S. Spa.
Flat Coated Retriever	F.C.Ret.	Spaniel	Spa.
Golden Retriever	G. Ret.	Staffordshire Bull Terrier	S.B.T.
Great Dane	G. Da.	Tibetan Terrier	Tib. T.
Greyhound	Grey.	Terrier	Ter.
Irish Setter	I. Set.	West Highland White Terrier	W.H.W.
Jack Russell Terrier	J.R.T.	Wire Haired Dachshund	W.H. Dach.
King Charles Spaniel	K.C.S.	Wire Haired Fox Terrier	W.H.F.T.
Labrador	Lab.	Yorkshire Terrier	York. T.

Normal Dogs (Group N)

The definition of a normal dog for the purpose of this thesis is that of a dog from the local canine population which was not showing signs of physical ill-health or behavioural abnormality and whose nutritional status appeared normal, although 3 were overweight (numbers N3, N10 and N16) and 2 were slightly overweight (numbers N12 and N13). The group consisted of 68 dogs. Some of the dogs (7) were colleagues' pets and another 20 were available for examination at the Edinburgh Dog and Cat Home through the courtesy of the Home's Consultant Veterinary Surgeon. The largest group (41) consisted of dogs which had minor injuries or which had recovered some time before from non-medical conditions and which now showed no abnormality but were available for examination. It also included normal dogs brought by the police.

Table 3 sets out the breed, age, sex and weight of the normal dogs.

The 68 dogs consisted of 19 different breeds or breed types (see Table 4), with from 1 to 10 dogs in each breed. The dogs were of the following sexes:

	M	Mn	F	Fn	Total
Number	36	2	28	2	68
Percentage	52.9	2.9	41.2	2.9	100

The age groups were as follows:

Age:	<6m	6-11m	1y	2y	3y	4y	5y	6y
No.:	4	9	12	5	11	3	5	5
Age:	7y	8y	9y	10y	11y	12y	13y	14y
No.:	2	1	0	2	1	0	0	1

Table 3

Normal Dogs: breed, sex, age and weight

Dog No.	Breed	Sex	Age (years)	Weight (kg)
N 1	Terrier	M	Adult	
N 2	F. C. Retriever	M	3 6/12	
N 3	Cairn	M	6	13.5
N 4	Terrier X	M	2	12.3
N 5	Greyhound	F		24.6
N 6	Collie X	M	3	10.6
N 7	Deerhound	M	2 2/12	34
N 8	Alsatian	M	5	
N 9	Terrier	F	10/12	13.4
N10	Cairn	Fn	7	10.5
N11	Collie X	F	8/12	10.5
N12	Poodle	M	3 6/12	9.5
N13	Labrador X	Mn	5	20
N14	Terrier X	M	6	11.5
N15	Collie X	F	6	10
N16	Irish Setter	F	4	28.5
N17	Greyhound	M	3	
N18	I. Labrador	Fn	5	25
N19	Lurcher	M	11/12	
N20	Alsatian	M	6	
N21	Labrador	F	3	
N22	Labrador X	M	3	
N23	Greyhound	F	3	23.5
N24	Terrier	M	old	
N25	B. Collie	M	4/12	
N26	Terrier	M	3	
N27	Terrier	M	9/12	
N28	S. Spaniel	F	4	
N29	Labrador	F	6	23
N30	Labrador	M	1	
N31	Greyhound	M	3	28
N32	Greyhound	F		21
N33	Boxer	M	adult	
N34	Boxer	F		
N35	F.C. Retriever	F	2	30
N36	Labrador	M		24
N37	Labrador	M	1	20
N38	Dalmatian	M	1	25
N39	Terrier	F	3	15-20
N40	Lurcher	F	4/12	10
N41	Collie X	F	5/12	15
N42	Collie X	F	6/12	15-20
N43	Collie	M	1 2/12	12-15
N44	Collie X	M	6/12	15-20
N45	Collie X	F	3 6/12	5-6
N46	Lurcher	M	6/12	10-15
N47	Terrier X	F	1 6/12	10-15

Table 3 (contd.)

Dog No.	Breed	Sex	Age (years)	Weight (kg)
N48	Terrier X	F	10/12	10-15
N49	Terrier	M	1	20
N50	WHW	F	1 6/12	7
N51	Terrier X	M	1 2/12	
N52	J.R. Terrier	M	1 6/12	
N53	Collie X	F	5/12	
N54	Collie X	F	10/12	
N55	Dalmatian	M	5 6/12	
N56	Labrador X	F	14	22.5
N57	Collie X	M	2	15
N58	Labrador X	F	1 3/12	
N59	J.R. Terrier	M	1 6/12	
N60	Dalmatian	M	4	
N61	Cairn Terrier	M	10	
N62	Alsatian	F	7	
N63	Boxer X	M	10	
N64	Irish Setter	F	5	
N65	Collie	F	1 3/12	
N66	Spaniel	F	11	
N67	Golden Retriever	Mn	2 9/12	
N68	Labrador	M	8	

M: male Mn: neutered male F: female Fn: neutered female

Table 4

Normal Dogs: number and percentage of each breed

Breed	Number	Percentage
Collie	10	14.7
Labrador	7	10.3
Terrier	7	10.3
Greyhound	5	7.4
Terrier X	5	7.4
Labrador X	4	5.9
Alsatian	3	4.4
Border Collie	3	4.4
Cairn Terrier	3	4.4
Dalmatian	3	4.4
Lurcher	3	4.4
Boxer	2	2.9
F C. Retriever	2	2.9
Irish Setter	2	2.9
J R Terrier	2	2.9
S Spaniel	2	2.9
Boxer X	1	1.5
Deerhound	1	1.5
Golden Retriever	1	1.5
Poodle	1	1.5
W H W	1	1.5
Total	68	100

The age of 7 dogs was not precisely known but 4 were young dogs (i.e. less than 2 years approximately) and the remaining 3 were mature adults, one of them being old. The age range was from 4 months to 14 years with most of those of known age being from 1 to 7 years.

The weight was recorded for 36 of the dogs and the range was 5 to 34 kg.

Dogs with Suspected Hypothyroidism (Group HS)

Some of the dogs entering the Small Animal Clinic as outpatients or brought into the Department of Medicine's Hospital as inpatients were referred by the receiving veterinary surgeon to the author as 'possible' cases of hypothyroidism, on the basis of the history and preliminary clinical examination. The author then recorded a detailed history and undertook a full physical examination of those patients. The pattern of the examination is shown in Table 5 . The sites of skin and hair abnormalities were recorded on charts (see Figure 1). Where hypothyroidism still appeared to be the most probable diagnosis on these grounds, and where the clinical evidence did not support or clearly suggest another diagnosis, these dogs were regarded as being cases of suspected clinical hypothyroidism.

Twelve of the suspected cases had been previously examined by members of the School or other veterinary surgeons and these dogs either were, or had been, on thyroid therapy. The remaining cases were new.

TABLE 5

Outline of form used for patients

Owner's name Address Case Number
Home tel. no.
Business "
Animal's name Sex Age Colour Weight
Breed

Primary complaint

Referred by Address

MEDICAL HISTORY

1. Previous illness and duration
2. Drugs given previously

PHYSICAL EXAMINATION

1. General appearance
2. Nutritional status Appetite Thirst
3. Mucous membrane
4. Temperature
5. Pulse rate
6. Superficial lymph gland
7. Eyes - normal discharge other lesion
8. Ears - normal rubbing head shaking
   discharge other lesion smell
9. Respiratory system
10. Alimentary system
11. Urinary system
12. Genital system
13. Musculo-skeletal system
14. Nervous system
15. Skin

Normal	Inflamed	Pruritus	Loss of hair
Alopecia	Hyperpigmentation	Hair easily epilated	Hyperkeratosis
symmetric			
assymetric	Lichenification		
Erythema		Excoriation	Macules
Papules	Pustules	Vesicles	Wheals
Nodules	Tumours	Scales	Crusts
Licking	Rubbing	Hot	Cold
Normal temp.	Bites	Wounds	Ectoparasites
Fleas	Lice	Ticks	Demodex
Sarcoptes	Others		

Bacteria: Culture and sensitivity

Resistant to:
Sensitive to:

Fungi Woods light KCH Culture

Character of hair and coat

Site of lesion(s)

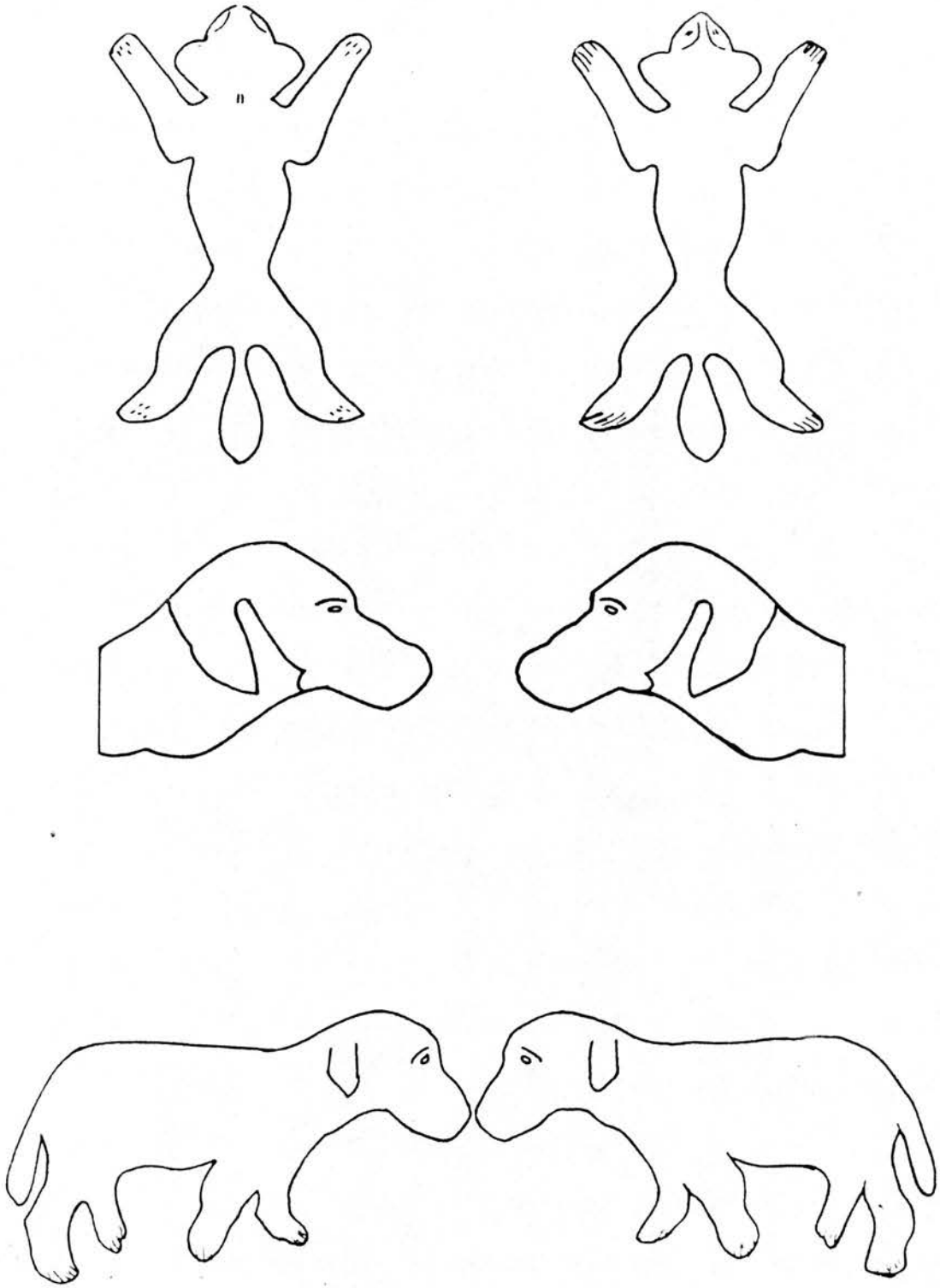


Figure 1 Diagram for depicting affected areas of skin and hair

The two-stage process, i.e. first of noting the 'possible' cases, then identifying the suspected cases, resulted in 47 cases of suspected clinical hypothyroidism being selected.

As the findings from history taking and physical examination constitute an important part of the clinical investigation, these records are dealt with in the Results section of the thesis and discussed later. However, at this stage it is convenient to state that the clinical criteria used were those generally accepted and published as indicative of hypothyroidism (see section on Clinical Hypothyroidism in the review of the literature).

The breed and sex of each case of suspected hypothyroidism and the dog's age and weight when it was first examined by the author are given in Table 6 .

Table 7 records the number of male, female and neutered dogs by breed.

The age range was 10 weeks to 13 years, weights ranged from 2.5 kg to 47 kg and the 47 dogs were of 22 breeds.

Cases of Other Hormonal Disease: Group OH

A major consideration in the diagnosis of clinical hypothyroidism is its differentiation from other diseases which share with it some common clinical features but which also have other unshared features. Quite apart from the difficulty of diagnosing canine hypothyroidism on clinical grounds beyond the stage of a presumptive diagnosis or, as

Table 6

Suspected Hypothyroid Cases: breed and sex; age and weight when first examined

Dog No.	Breed	Sex	Age (years)	Weight (kg)
HS 1	Airedale	M	8	28
HS 2	Poodle	M	13	12.4
HS 3	Boxer	Fn	4	23
HS 4	Dachshund	F	2	11
HS 5	Labrador	F	2	35
HS 6	Labrador	F	3	30
HS 7	W H Dachshund	F	7 6/12	12
HS 8	W H W	M	12	12
HS 9	Poodle	M	12	8.5
HS10	Poodle X	Fn	12	8
HS11	W H W	F	8	9.5
HS12	Cairn	F	13	5.9
HS13	Airedale	M	10	34
HS14	Scottish Terrier	F	3	11
HS15	Labrador	M	4 6/12	33
HS16	Airedale	F	3	34
HS17	Labrador	F	7	34
HS18	Yorkshire Terrier	Fn	9	3
HS19	Labrador	F	5 9/12	31.5
HS20	Doberman	F	11	29.5
HS21	W H W	M	6	13
HS22	Yorkshire Terrier	M	3	3.5
HS23	Irish Setter	M	2	35
HS24	P M D	F	10 weeks	42
HS25	Cairn	F	12	7
HS26	S H Fox Terrier	F	7	9
HS27	Shetland Collie	F	4	10.5
HS28	Cairn	F	2 6/12	7.5
HS29	Collie X	F	11	26.5
HS30	Chow Chow	M	4/12	16
HS31	Corgi	M	10 9/12	12.5
HS32	Labrador	F	7	30.5
HS33	W H W	F	9	8.5
HS34	Cairn	F	7	9.5
HS35	Lakeland Terrier	F	12	12
HS36	Poodle	F	9	11
HS37	Beagle	M	9	24
HS38	Tibetan Terrier	M	10	11.5
HS39	Doberman	M	7	42
HS40	Golden Labrador	F	6	
HS41	Doberman	F	8	31.8
HS42	Scottish Terrier	F	3	
HS43	Dachshund	F	10	
HS44	Spaniel	M	10	20.5
HS45	Irish Setter	F	9	37.5
HS46	Labrador	Mn	3	
HS47	Irish Setter	F	7	28.5

M: male Mn: Male neutered F: female Fn: female neutered

Table 7

Suspected Hypothyroid Cases: number of each breed and number of each sex

Breed	Male	Mn	Female	Fn	Total
Labrador	1	1	6	-	8
Cairn	-	-	4	-	4
W H W	2	-	2	-	4
Airedale	1	-	2	-	3
Doberman	1	-	2	-	3
Dachshund	-	-	3	-	3
Irish Setter	1	-	2	-	3
Poodle	2	-	1	-	3
Yorkshire Terrier	1	-	-	1	2
Scottish Terrier	-	-	2	-	2
Beagle	1	-	-	-	1
Boxer	-	-	-	1	1
Collie X	-	-	1	-	1
Chow Chow	1	-	-	-	1
Corgi	1	-	-	-	1
Lakeland Terrier	-	-	1	-	1
Poodle X	-	-	-	1	1
P M D	-	-	1	-	1
S H Fox Terrier	-	-	1	-	1
Shetland Collie	-	-	1	-	1
Spaniel	1	-	-	-	1
Tibetan T.	1	-	-	-	1
Total	14	1	29	3	47
Percentage	29.8	2.1	61.7	6.4	100

M: male Mn: male neutered F: female Fn: female neutered

is preferred in this thesis, as a case of suspected hypothyroidism, there are difficulties even when laboratory methods of examination are also employed. These factors also apply to the diagnosis of other endocrine disorders of the dog. Nonetheless, it is commonplace for the diagnosis of certain of these other hormonal disorders to be made mainly on grounds of the history, age, sex and physical examination of the patient. Frequently the endocrinological assays that would lead from a presumptive to a confirmed diagnosis are not available. More often, laboratory tests of a non-specific kind are employed and while they do not give a specific diagnosis they may strengthen the clinical opinion. Other tests may be positive for certain conditions other than the one suspected and this may also help in diagnosis, at least by eliminating some possibilities.

This preamble is necessary, as the next group of dogs to be discussed is defined as consisting of cases of "other hormonal diseases" or hormonal diseases other than those associated with thyroid disfunction, especially hypothyroidism. For most of the cases included here, the presumptive diagnosis is based on the collective clinical experience of the veterinary staff of the Department of Veterinary Medicine and the Small Animal Clinic.

The author then undertook the further clinical examinations and laboratory tests that are reported elsewhere in the thesis. Thus, this group includes dogs with

dermatoses that on clinical or preliminary laboratory examinations were considered not to be due primarily to external parasites, bacteriological infections or allergic responses. The dogs of this group did not manifest the combination of clinical findings classically associated with hypothyroidism and they sometimes showed signs that were classically associated with certain other hormonal disorders. Included in this group were cases considered to be Cushing's disease, iatrogenic Cushing's disease and defective functioning of male and female gonads.

However, while they are described as cases of hormonal disease, the definitive diagnosis is often not known. This group is decribed as Group Other Hormonal or OH.

Table 8 gives the breed, sex, age and weight of these dogs. The proportions of the different breeds are given in Table 9 The number of each sex is given in Table 10 . The age groups are shown in Table 11.

The OH group consisted of 47 dogs of 24 breeds or types, aged from 4.5 months to 14.5 years. The weights range from 4.5 to 43 kg for 34 of the dogs and 16 of these were considered to be overweight.

Dogs with Non-Hormonal Skin Conditions (Group NH)

From the cases entering the clinic or hospital, a number of dogs with skin diseases of apparently non-hormonal aetiology were referred by members of the School staff to

Table 8

Group: Other Hormonal (OH): breed, sex, age and weight

Dog No.	Breed	Sex	Age (years)	Weight (kg)
CH 1	Cairn	M	9	
OH 2	Irish Setter	M	3	43
CH 3	Jack Russell Terrier	M	5	9
OH 4	W H W	M	14 6/12	9
OH 5	Whippet	M	8	12.3
OH 6	Shetland Collie	M	12	
OH 7	Lakeland Terrier	M	8	
OH 8	W H W	F	8	9.5
OH 9	Pekinese	F	14	7
OH10	Poodle	Mn	12 6/12	17.5
OH11	Golden Retriever	M	8	30
OH12	Poodle	F	6	7
OH13	Golden Retriever	F	6	29
OH14	Keeshound	F	5	16.5
OH15	Pug	F	3 9/12	
OH16	W H W	M	4	6.5
OH17	W H W	F	6	8.5
OH18	Collie X	Fn	7	17
OH19	Labrador	F	1 2/12	21
OH20	Collie	F	9 6/12	24
OH21	Labrador	Fn	5	27
OH22	Spaniel	F	9 6/12	14
OH23	Boxer	F	3	27.5
OH24	Cairn	M	11	10
OH25	Terrier	M	8	18.5
OH26	Dandie Dinmont	F	1	7.5
OH27	Spaniel X	F	4 6/12	17.5
OH28	Beagle	M	12	
OH29	Pug	Fn	8 6/12	11
OH30	Labrador	Mn	1 6/12	30
OH31	Labrador	Mn	8	46
OH32	W H W	Mn	7	9.5
OH33	Poodle	F	18 weeks	
OH34	Shetland Collie	M	9	
OH35	Border Terrier	M	7 6/12	13
OH36	Boxer	Fn	7	25
OH37	Scottish Terrier	F	5 6/12	19
OH38	Yorkshire Terrier	M	2 6/12	4.5
OH39	Scottish Terrier	M	2 4/12	
OH40	Collie	M	10	
OH41	Spaniel	M	1 8/12	20.5
OH42	Border Terrier	M	10	10
OH43	Spaniel	F	7	17.4
OH44	King Charles Spaniel	F	9	
OH45	Border Collie	M	5 6/12	
OH46	Pomeranian	M	8	
OH47	Labrador X	F	10	

M: male Mn: male neutered F: female Fn: female neutered

Table 9

Group Other Hormonal (OH): number and percentage of each breed

Breed	No. of each breed	Percentage
W H W	5	10.6
Labrador	4	8.6
Collie	3	6.4
Poodle	3	6.4
Spaniel	3	6.4
Border Terrier	2	4.3
Boxer	2	4.3
Cairn	2	4.3
Pug	2	4.3
Retriever	2	4.3
Scottish Terrier	2	4.3
Shetland Collie	2	4.3
Beagle, Collie X, Dandie Dinmont, Irish Setter, Jack Russell Terrier, Keeshound, King Charles Spaniel, Labrador X, Lakeland T, Pekinese, Pomeranian, Spaniel X, Terrier, Whippet, Yorkshire T, of each	1	15 x 2.12
Total	47	

Table 10

Group Other Hormonal (OH): number of each sex

Sex	Male	Male neutered	Female	Female neutered	Total
No.	21	4	18	4	47
%	44.7	8.5	38.3	8.5	

Table 11

Group OH: age of dog with 'other hormonal' conditions when presented

Age	< 6m	6-11m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y	11y	12y	13y	14y	Total
No. of																	
Male			1	2	1	1	2		1	5	2	2	1	2		1	21
Male n			1						1	1				1			4
Female	1		2		2	1	2	3	1	1	3	1				1	18
Female n							1		2	1							4
Total	1		4	2	3	2	5	3	5	8	5	3	1	3		2	47

the author who then subjected each case to the form of clinical examination and recording described in connection with the suspected hypothyroid cases. As seemed appropriate from these clinical findings, further examinations were then conducted such as microscopic examination of skin scrapings for external parasites, skin swabbing for bacterial culture, faecal examination, urinalysis, haematology, biochemical examination of blood and urine, examination of hair for stage of growth, double skin thickness measurements and histopathological examination.

As a result of the clinical examination and aids to diagnosis, cases were placed in three categories, namely pyoderma, allergic dermatosis, and external parasitism, and assigned identification numbers with the letters P, A and EP respectively.

The three groups consisted of 99, 57 and 49 dogs respectively, a total of 205 dogs (see Table 1).

Cases of Pyoderma: Group NH,P

This group is referred to for convenience as Group Non-Hormonal, Pyoderma or Group NH,P, or Group P.

These dogs had inflammatory skin lesions ranging from chronic to acute in duration, from active to quiescent in nature, from mild to severe in degree and from local to general in distribution.

Pruritis was a very frequent finding especially in the cases of progressive, severe dermatosis. Hair loss was also

commonly observed and occurred at discrete, unilateral sites and bilaterally. Most of the chronic cases had hyper-pigmentation of the skin and in some of the chronic cases the skin was thickened.

Some cases had mild or chronic external otitis of varying degrees of severity. Some cases had interdigital pyoderma either alone or in conjunction with other skin lesions, and acute moist dermatitis and labial dermatitis were also observed.

In addition to these signs directly associated with the skin, some dogs were lethargic, sleepy, easily tired and/or greedy. Other signs present in a few dogs included polydipsia, polyuria, cold body surface apart from inflamed areas, and/or a puffy appearance of the eyelids. However, the predominating clinical feature was an inflamed skin.

Group P contained 99 dogs from 32 breeds or types. Table 12 gives the breed, age, sex and weight of each dog. The numbers of each breed and of each sex are given in Tables 13 and 14 respectively. Table 15 sets out the number at different ages.

The ages ranged from 8 weeks to 15 years; the body weights ranged from 2.5 kg to 58 kg in the 63 cases in which it was recorded. Of those, 36 had weights regarded as normal for their breed and age, 27 were overweight and 1 was slightly overweight.

In addition to the detailed physical examination of these cases, and the microbiological examinations kindly undertaken

Table 12

Group non-hormonal, pyoderma (P): breed, age, sex and weight

Dog No.	Breed	Sex	Age (years)	Weight (kg)
P 1	S. Spaniel	F	5	
P 2	Labrador X	F	2 6/12	24.5
P 3	Terrier X	F	7 6/12	16.5
P 4	Spaniel	F	6	16
P 5	Terrier	M	12	16.5
P 6	W H W	M	8 6/12	8
P 7	W H W	M	9	10.5
P 8	Labrador	M	4	22.2
P 9	Terrier	M	8	12.5
P10	B. Collie	M	1 3/12	17
P11	Terrier	M	3 6/12	14.5
P12	P M D	M	4	65
P13	Cairn	M	6	7.5
P14	Alsatian	M	3	45.5
P15	Golden Retriever	M	3	
P16	Great Dane	M	1 6/12	45.5
P17	Lurcher	M	6/12	24.7
P18	Boxer	M	5 6/12	33.8
P19	Old English Sheepdog	M	3	26.3
P20	W H W	M	9 9/12	12.5
P21	Cairn	M	2	8.5
P22	P M D	M	3	36.3
P23	M. Poodle	F	6	11
P24	W H W	Fn	11	9.5
P25	Yellow Labrador	F	2	23
P26	Alsatian	F	3 6/12	
P27	Shetland Collie	M	12	
P28	Boxer	M	10	25
P29	Airedale	M	15	
P30	W H W	M	4/12	4.5
P31	Golden Retriever	M	10	
P32	W H W	M	6	11
P33	Border Terrier	M	4	
P34	W H W	Fn	7	
P35	Irish Setter	F	4	29.5
P36	Black Labrador	M	1 6/12	28
P37	Cairn	M	1	
P38	Terrier	M	11	
P39	Border Collie	M	8 4/12	
P40	W H W	Mn	14	5
P41	W H W	M	2	10
P42	W H W	F	8	8
P43	Cairn	Fn	8 6/12	10.5
P44	Yorkshire Terrier	F	8/12	2.5
P45	Collie	M	8/12	

Table 12 (contd.)

Dog No.	Breed	Sex	Age (years)	Weight (kg)
P46	Pekinese	M	7 4/12	5
P47	Spaniel	M	6	
P48	W H W	M	8	8.7
P49	Poodle	F	7 6/12	
P50	Shetland Collie	M	8	8.5
P51	Beagle	M	4	
P52	S.B. Terrier	Fn	10	14.5
P53	Scottish Terrier	F	6	11
P54	Labrador X	F	4	
P55	E. Setter	F	4	
P56	Alsatian	F	9	34.5
P57	Labrador X	M	4 6/12	37.5
P58	W H W	M	9 9/12	10
P59	Cairn	F	8	10
P60	W H W	M	12	8.75
P61	Yellow Labrador	F	4 6/12	26.5
P62	Basset	F	4 6/12	
P63	Yellow Labrador	M	8	
P64	Collie	M	4 6/12	20
P65	W H W	M	2 6/12	8.5
P66	Yellow Labrador	F	5 6/12	
P67	Alsatian	F	5	31
P68	W H W	F	9/12	
P69	Pekinese	F	6 6/12	4.5
P70	Alsatian	M	8	
P71	Spaniel	F	3 6/12	
P72	Yellow Labrador	F	3 6/12	28.5
P73	Doberman	M	1	26
P74	Great Dane	F	13 weeks	
P75	Poodle	F	5	9.5
P76	Labrador X	F	8 weeks	
P77	Terrier	M	6/12	15.5
P78	Black Labrador	F	2	24
P79	Labrador X	M	10	
P80	English Setter	F	1 6/12	27
P81	Irish Setter	F	1 2/12	
P82	Labrador	M	1	29
P83	Alsatian	F	1 6/12	32.5
P84	W H W	M	15	9.5
P85	Pug	M	8	9.5
P86	P M D	M	3	58
P87	Doberman	M	10	
P88	Whippet	M	2	
P89	Keeshound	M	6	
P90	Jack Russell Terrier	F	4 6/12	
P91	W H W	M	9/12	7
P92	W H W	F	8/12	6
P93	Great Dane	F	4 6/12	43.5
P94	Beagle X	F	9	
P95	Alsatian	M	5/12	
P96	Irish Setter	M	1	
P97	W H W	M	10 6/12	
P98	Cocker Spaniel	M	6/12	13
P99	Dachshund	M	9	

Table 13

Group NHP: the number of each breed or type affected with pyoderma

Breed	Number
W H W	19
Labrador	9
Alsatian	7
Cairn	5
Labrador X	5
Spaniel	5
Terrier	5
Collie	4
Irish Setter	3
Great Dane	3
P M D	3
Poodle	3
Boxer	2
Doberman	2
English Setter	2
Golden Retriever	2
Pekinese	2
Shetland Collie	2
Airedale, Basset, Beagle, Beagle X, Border Terrier, Dachshund, Jack Russell Terrier, Keeshound, Lurcher, Old English Sheepdog, Pug, Scottish Terrier, S.B. Terrier, Terrier X, Whippet, Yorkshire Terrier of each	1
Total	99

Table 14

Group NH,P: number of each sex of dog with pyoderma

Sex	M	Mn	F	Fn	Total
No.	59	1	35	4	99
%	59.6	1.0	35.4	4.0	100

Table 15

Group NH,P: age of dogs with pyoderma when presented

Age	< 6m	6-11m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y	11y	12y	13y	14y	15y	Total
M	2	6	7	4	6	6	1	4	1	8	4	5	1	3			1	59
Mn																1		1
F	2	3	3	3	3	7	4	4	2	2	2							35
Fn									1	1		1	1					4
Total	4	9	10	7	9	13	5	8	4	11	6	6	2	3	-	1	1	99

M: male Mn: Male neutered F: female Fn: female neutered

in the Department of Pathology, other investigations were conducted on these patients and these are described and reported in the section of the thesis dealing with experimental work.

Swabs were taken from the skin lesions and, in the Department of Pathology of the Royal (Dick) School of Veterinary Studies, were cultured and subjected to in-vitro sensitivity tests against various therapeutic substances. The commonest organism to be isolated was Staphylococcus aureus. Isolations were made very much less frequently of unidentified gram negative coccobacilli, yeasts of Pityrosporum type, beta-haemolytic group G streptococci, Pseudomonas aeruginosa, Staphylococcus epidermidis, alpha-haemolytic streptococci, diptheroids and members of the genus Proteus. In a few cases, the presence of bacterial infection was not demonstrated.

Dogs with Allergic Skin Conditions (Group NH,A)

Members of the staff of the Clinic and Hospital referred cases of suspected allergic skin conditions to the author. These cases were already diagnosed before referral. Diagnosis was based on such information and observations as the occurrence of seasonal dermatosis, known contact with certain substances in the dogs' environment, pruritus and pulling out of hair, with hyperaemia and excoriation of the skin, by biting and rubbing. This sometimes led to areas of alopecia. Some dogs had papules or other rashes either

diffusely over the body or on the ventral surface. Some cases described as pruritic by the owners had no obvious lesions.

Skin scrapings were made from most of the cases. They were negative on microscopic examination for external parasites. Some cases had skin sensitivity tests conducted. In cases which appeared to be complicated by infection, bacteriological cultures and antibiotic sensitivity tests were made. The presence of infection, especially in cases of some duration, worsened the condition and added to the difficulty in diagnosis. However, in most cases, the presumptive diagnosis of allergy was made fairly readily on the history, the distribution and nature of the lesions and the absence of external parasites. The response to therapy, including exclusion from the suspected item or environment, was also taken into account.

Table 16 sets out the breed, age, sex and weight of the dogs assigned to this category. The number of each breed is shown in Table 17 and the number of each sex in Table 18. The numbers in each age group are shown in Table 19.

There were 57 dogs of 23 breeds and types in this category. Their ages ranged from 3 months to 13 years and 6 months. The weight was recorded in 36 cases. It ranged from 6 - 43 kg. Twelve of the dogs were considered to be overweight with a further 2 slightly overweight.

The dogs with presumptive allergic disorders of the skin comprise Group Non-Hormonal, Allergic, i.e. Group NH,A

Table 16

Group Non-hormonal, Allergic (NH,A): breed, age, sex and weight

Dog No.	Breed	Sex	Age (years)	Weight (kg)
A 1	Collie	Fn	6	21.5
A 2	Collie	Fn	6	24.5
A 3	Terrier	M	6	
A 4	Yellow Labrador	F	5 6/12	28
A 5	Shetland Collie	M	5 6/12	7.7
A 6	Jack Russell Terrier	M	1 6/12	7.5
A 7	Shetland Collie	M	5 6/12	13.5
A 8	Yellow Labrador	M	2 6/12	33
A 9	Terrier	F	3	18
A10	Doberman	M	5 6/12	33
A11	Poodle	M	5	6
A12	Terrier X	M	5	25
A13	Labrador X	M	7	15
A14	Poodle	M	6	9.5
A15	Terrier	Mn	13 6/12	23.5
A16	W H W	F	11/12	7.3
A17	Old English Sheepdog	F	2 6/12	
A18	Golden Retriever	F	3/12	25
A19	Alsatian	F	6	33
A20	Boxer	Fn	6 6/12	25.5
A21	W H W	F	3	
A22	Pointer	F	4	
A23	Cairn	M	13	8.5
A24	Cairn	M		9
A25	Border Terrier	Mn	8	12
A26	Yellow Labrador	F	3	
A27	Yellow Labrador	M	2 6/12	
A28	English Setter	M	7/12	
A29	Labrador	M	1 4/12	33.5
A30	Boxer	F	1	19
A31	Golden Retriever	M	9	35.5
A32	Cairn	M	13	
A33	Yellow Labrador	M	7 6/12	
A34	Bearded Collie	Fn	5	16.5
A35	Doberman	F	1 6/12	
A36	B. Labrador	Fn	3	
A37	Golden Retriever	F	6	
A38	Labrador X	F	4/12	
A39	Poodle	F	1	
A40	Labrador X	F	4	23
A41	Alsatian	F	2	
A42	Collie X	M	6	
A43	Alsatian	Mn	6 8/12	42
A44	Labrador	F	4	20
A45	Golden Retriever	M	11/12	
A46	Great Dane	Fn	7	43

Table 16 (contd.)

Dog No.	Breed	Sex	Age (years)	Weight (kg)
A47	B. Labrador	M	10	
A48	Labrador	F	8 6/12	19
A49	Shetland Collie	F	4 6/12	13
A50	Corgi	Fn	1 8/12	15
A51	Lakeland Terrier	Fn	1	7
A52	Keeshound	F	3	19
A53	Alsatian	F	1	
A54	Shetland Collie	Fn	3 6/12	7.8
A55	Boxer X	F	10	11
A56	Golden Retriever	F	2 6/12	
A57	Boxer	M	10	

Table 17

Group NH, A: the number of each breed or type affected with allergic skin conditions

Breed	No. of each breed	Percentage
Labrador	10	17.5
Retriever	5	8
Alsatian	4	7
Shetland Collie	4	7
Boxer	3	5.3
Cairn	3	5.3
Labrador X	3	5.3
Poodle	3	5.3
Terrier	3	5.3
Collie	2	3.5
Doberman	2	3.5
W H W	2	3.5
Bearded Collie, Border Terrier, Boxer X, Collie X, Corgi, English Setter, Great Dane, Jack Russell Terrier, Keeshound, Lakeland Terrier, Old English Sheepdog, Pointer, Terrier X of each	1	13 x 1.8
Total	57	100

Table 18

Group NH,A: number of each sex of dogs with allergic skin conditions

Sex	Male	Male neutered	Female	Female neutered	Total
No.	22	3	23	9	57
%	38.6	5.3	40.4	15.8	

Table 19

Group NH,A: age of dogs with allergic skin conditions when presented

Age	< 6m	6-11m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y	11y	12y	13y	Age unknown	Total
M		2	2	2			5	3	2		1	2			2	1	22
Mn								1		1					1		3
F	2	1	4	3	4	4	1	2		1		1					23
Fn			2		2		1	3	1								9
Total	2	3	8	5	6	4	7	9	3	2	1	3			3	1	57

M: male Mn: male neutered F: female Fn: female neutered

or Group A.

Cases of External Parasitism (NH,EP)

Dogs were referred to the author in the usual way from the Clinic and Hospital as cases of dermatoses.

In the absence of history or clinical findings suggestive of alternative diagnoses, a diagnosis of external parasitism was made on the basis of the visual demonstration of flea or lice infestation or by the demonstration of mites on the microscopic examination of skin scrapings, coat brushings or ear swabs. In some cases parasites were not observed, and in these cases the diagnosis was based on the appearance of the lesions, e.g. the presence of flea bite reactions or the thickening of the ear margin in sarcoptic mange. The response to appropriate therapy was taken into account diagnostically at a later stage of consideration of the case.

The breed, sex, age and weight of each dog, and the diagnosis made, are given in Table 20 .

Tables 21 and 22 set out the numbers of dogs involved, by breed and sex, respectively.

The distribution of ages is shown in Table 23 .

A diagnosis of external parasitism was made in 49 cases, involving 26 breeds. The age range of the affected dog was from 10 weeks to 12 years. The weight of 24 dogs, in which it was recorded, ranged from 3 to 29.5 kg. In an expression of opinion regarding obesity, it was considered that 7 of the dogs were overweight.

Table 20

Group NH,EP: breed, age, sex, weight and diagnosis of dogs with ectoparasitism

Dog No.	Breed	Sex	Age (years)	Weight (kg)	Diagnosis
EP 1	Shih Tzu	M	1 6/12	6.7	D
EP 2	Dachshund	F	3 6/12		D
EP 3	Cairn	F	9	10.8	D
EP 4	W H Fox Terrier	F	2	6.5	D
EP 5	Terrier	F	6/12	8.7	D
EP 6	Labrador X	F	1	20.5	D
EP 7	King Charles Spaniel	F	10 weeks	3	S
EP 8	Irish Setter	M	5 6/12	31	S
EP 9	Labrador	F	5	34.5	S
EP10	Alsatian	M	9/12		S
EP11	Shetland Collie	F	8		C
EP12	Jack Russell Terrier	F	1		D
EP13	Golden Retriever	M	7		S
EP14	King Charles Spaniel	F	5 6/12	4.5	S
EP15	Y. Labrador	F	1 2/12	19	S
EP16	Labrador	M	3		S
EP17	Doberman	M	7/12		D
EP18	W H W	M	12		T
EP19	Lurcher	F	9/12		S
EP20	English Setter	F	3	23	O
EP21	Collie	F	2		S
EP22	Terrier	Fn	8	10.5	C
EP23	Boxer	M	12 weeks	17.5	S
EP24	Terrier X	M	12 weeks		S
EP25	Collie	M	3/12	6.5	S
EP26	Collie X	F	3 5/12	29.5	D
EP27	Greyhound	M	1 8/12		S
EP28	Spaniel	F	6	15.3	D
EP29	Scottish Terrier	F	2 6/12	7.8	D
EP30	Spaniel	M	6/12		D
EP31	Collie	F	2 6/12	19.5	F
EP32	Retriever	M	1 4/12		F
EP33	Spaniel	M	3	12.5	L
EP34	Beagle	M	3		F
EP35	W H W	M	3	7.25	F
EP36	Spaniel	M	6/12	16	F
EP37	Boxer	Fn	5 6/12	20.5	F
EP38	Terrier	F	5		F
EP39	Spaniel	F	5	18	L
EP40	Poodle	M	1 3/12	6.5	F
EP41	Labrador	F	6 9/12		F
EP42	F.C. Retriever	M	10		F
EP43	Labrador	M	5		L
EP44	Basset	M	2		L

Table 20 (contd.)

Dog No.	Breed	Sex	Age (years)	Weight (kg)	Diagnosis
EP45	Alsatian	F	1 1/12		D
EP46	Boxer	M	7/12		D
EP47	Boxer	M	12		D
EP48	Retriever	M	6		C
EP49	Jack Russell Terrier	M	9/12		C

M: male Mn: male neutered F: female Fn: female neutered

Diagnosis: C: Cheyletiella yasguri
D: Demodectic mange
F: Flea infestation
L: Lice infestation
O: Otodectes cynotis (earmites)
S: Sarcoptic mange
T: Trombicula autumnalis

Table 21

Group NH,EP: the number of each breed or type affected with external parasitism

Breed	Number	Percentage
Labrador	5	10.2
Spaniel	5	10.2
Boxer	4	8.2
Collie	3	6.1
Golden Retriever	3	6.1
Terrier	3	6.1
Alsatian	2	4.1
King Charles Spaniel	2	4.1
Jack Russell Terrier	2	4.1
W H W	2	4.1
Basset, Beagle, Cairn, Collie X, Dachshund, Doberman, English Setter, F C Retriever, Greyhound, Irish Setter, Labrador X, Lurcher, Poodle, Scottish Terrier, Shetland Collie, Shih Tzu, Terrier X, W H Fox Terrier, of each	1	18 x 2.0
Total .	49	

Table 22

Group NH,EP: number of each sex of dogs with external parasitism

Sex	Male	Male neutered	Female	Female neutered	Total
No.	25		22	2	49
%	51		44.9	4	100

Table 23

Group NH,EP: age of dogs with external parasitism when presented

Age	<6m	6-11m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y	11y	12y	13y	Total
M	3	6	4	1	4		2	1	1			1		2		25
Mn																
F	2	2	4	4	3		3	2		1	1					22
Fn							1			1						2
Total	5	8	8	5	7	-	6	3	1	2	1	1	-	2		49

M: male Mn: male neutered F: female FN: female neutered

SKIN THICKNESS

Introduction

Because of the frequent references to alteration in skin thickness in hypothyroid dogs, it was considered desirable to attempt to put this onto a more objective basis by making skin measurements in living dogs. The intention was to compare skin thickness in hypothyroid dogs with normal dogs and dogs with a variety of disease conditions.

Materials and Methods

Subjects

The skin thickness was measured in 84 dogs of 27 breeds. Most of them were outpatients of the clinic. Their diet and management varied as is usual with dogs kept as domestic pets. They were classified in 4 groups, by the nature of their disorder or normal state, as follows.

Group 1, Normal dogs. The skin of 35 normal, healthy dogs (21 male and 14 female) of 18 breeds, aged from 4 months to 14 years was measured. Their body weight

ranged from 7.7 to 42 kg, Individual details are given in Table 42.

Group 2, Hypothyroid dogs. 12 dogs (3 male and 9 female) of 9 breeds, aged from 10 weeks to 13 years were examined. They were diagnosed as cases of hypothyroidism. Body-weight ranged from 8 to 42 kg. Individual details are given in Table 43.

Group 3, "Other hormonal" cases. This group consisted of 7 dogs (4 male, 2 female and 1 neutered female) of 5 different breeds, affected with Cushing's syndrome, iatrogenic Cushing's syndrome, diabetes mellitus and one case of hepatic cirrhosis and one of overweight. These two last conditions were of unknown aetiology. The dogs were aged from 2 years 2 months to 13 years and their weights ranged from 6 to 30 kg. Details are in Table 44.

Group 4, Non-hormonal cases. This group consisted of 30 dogs (17 entire and 1 castrated male and 11 females and 1 neutered female), of 17 breeds, aged from 3 months to 12 years and weighing from 3 to 33.8 kg. These dogs had non-hormonal skin conditions such as bacterial or parasitic dermatoses and skin allergies. Details are in Table 45.

Skin Sites Measured

Skinfold thickness measurements were made at 15 different sites. These were lip, nose, eyelid, ear margin, ear pinna, throat, chest, axilla, abdomen, groin, lower part of leg, hip, withers, lumbar region and lumbo-sacral region.

Method of Measuring the Skin

The calipers used were calibrated in millimetres, (see Figure 8). A fold of skin was held between the fingers and the calipers gently placed on the skin fold and the measurement taken without either undue pressure or looseness of the calipers. The measurement which was of double skin thickness, was recorded in millimetres.

Statistical Analysis of Results

The statistical analyses employed are referred to at the appropriate stage in the results.

STAGES OF HAIR CYCLE IN HYPOTHYROID AND OTHER DOGS

Introduction

A number of workers have described the appearance and distribution of alopecia in a variety of endocrine imbalances and other occurrences in the dog. A few have reported on the proportion of anagen and telogen stages in normal dogs but little has appeared concerning these stages in hypothyroid dogs. Accordingly, it was considered desirable to investigate whether there were recognisable patterns in the proportions of hairs in the active stage of growth (anagen) and the resting stage (telogen) in canine hypothyroidism. The intention was to investigate whether information of this kind could be of value in diagnosing hypothyroidism in the dog or in its differential diagnosis from other conditions.

Material and Methods

Group One, Normal Dogs (A)

Ten dogs (NA1 to NA10), all considered to be normal healthy animals, were selected. They were fed on various brands of tinned dog food and household scraps. The dog's breed, age, sex and system of management is given

in Table 24. Hair samples were taken for examination from the dogs once monthly from December, 1977, to November, 1978.

Table 24

Group One, Normal Dogs, A (10). Hair examined at monthly intervals for 1 year.

No.	Breed	Age	Sex	Management
NA1	Labrador	3.5y	M	Household pet.
NA2	Labrador	10y	F	Kennels. Short walk daily.
NA3	Collie	7y	F	Household pet.
NA4	Poodle	5y	M	Household pet.
NA5	Dachshund	11y	M	Household pet.
NA6	Whippet	4.5y	M	Household pet.
NA7	Cairn	7.5y	M	Kennels. short walk daily.
NA8	Greyhound	6.5y	M	" " "
NA9	Collie	15y	F	" " "
NA10	Alsatian	10y	F	Household pet. Little out of doors.

M : Male F : Female

Group Two, Normal Dogs (B)

Each of a group of 10 normal dogs (NB1 to NB10) had hair examined on one occasion only. Their individual data are given in Table 53. These dogs were household pets on a variety of diets.

Group Three, Dogs with Hypothyroidism

Because of the difficulty in arranging for owners to attend the clinic frequently, it was not possible to examine the hair of cases of (suspected) hypothyroidism monthly.

The hair of 24 cases was examined but this was more than once in 8 cases only. Table 54 sets out the breed, age and sex of these dogs. They were household pets.

Group Four to Eight, Dogs with Other Conditions

These groups contained 47 dogs affected by various conditions, only some of which cause hair loss. Hypothyroid cases were not included. In 7 cases (Group 4) the disorders are not known to affect the hair. There were also 12 cases of hormonal disorders (Group 5), 16 cases of pyoderma (Group 6), 3 of allergic conditions (Group 7) and 9 of ectoparasites (Group 8). The data concerning these 5 groups of cases are set out in Tables 55 to 59 respectively.

At least 100 to 200 hairs were plucked from each dog from the dorsal aspect of the back and the ventral surface of the abdomen. In some dogs, the hairs were easily epilated but in others this was difficult. The hairs were placed on a glass slide and covered with tap water or glycerin, taking care to avoid air bubbles. Cover slips were employed. The microscopic field was examined under low power magnification and, in doubtful cases, under a higher power. The hairs in the anagen and telogen stages were counted. Figures 2, 3, 4 illustrate the anagen phase, Figure 4 shows hair in the stage of anagen described as metanagen by Chase (1965). This is followed by the catagen stage (not illustrated). Figures 5, 6, 7 illustrate hairs in telogen.

METHODS OF EXAMINATION

Bacteriological Examination

Sterile swabs were used to obtain material from the skin lesions in some cases, when on clinical grounds infection was suspected to be present. The swabs were submitted to the Applied Pathology Unit of the School for bacteriological examination. This included cultural identification and antibiotic sensitivity tests.

Examination of Skin Scrapings

Using a clean scalpel blade, deep skin scrapings were made in the normal fashion from one or more skin lesions. The material obtained was placed on a microscopic slide, a few drops of 10% KOH solution added, and the slide was gently warmed. A cover slip was put in place with gentle pressure to flatten the preparation, which was then examined microscopically under both low and high power objectives, in a search for mites and their ova.

Biochemical Examinations

Blood samples for the estimation of PBI, cholesterol, T3, T4, GOT, GPT and SAP were collected with the minimum of venous stasis into vacuum collection tubes (Vacutainer; Becton, Dickerson & Co., Drogheda, Ireland) and allowed to clot. As soon as the clot had retracted, the serum was separated and placed in sealed plastic containers. The part of each sample which was not for immediate assay (PBl, T3, T4) was stored at -20^{o}C.

Total Iodine and Protein Bound Iodine

These were estimated using a modified method of Benotti and Benotti (1963). Separation of the PBI from inorganic iodine was by treatment of the serum through Amberlite anion exchange resin 1KA 400 (cl).

The chloric acid digestion method introduced by Zak et al. (1952) and improved by O'Neal and Simms (1953) was used to destroy organic matter. The colorimetric measurement of ceric ions was simplified by using brucine sulphate to terminate the Ce^{+4} — As^{+3} reaction (Farrell and Richmond, 1961).

Serum Cholesterol

Serum cholesterol was estimated within 18 hours of collection using a Boehringer Cholesterol (Colorimetric Method) Test-Combination and an EEL Portable Colorimeter Filter 626 (560-580nm) (Corning-EEL Ltd., Halstead, Essex). The method was checked for specificity against a Boehringer Cholesterol Enzymatic Method No. 124 079 (Boehringer Corp., London).

Serum Glutamic Oxalacetate Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT)

These enzymes (synonyms: aspartate aminotranferase, AST, and alamine aminotransferase, ALT) were assayed using Calbiochem Stat-Pak (Hoechst, U.K., Ltd.) at 30°C and read in a Cecil 292 Spectrophotometer (Cecil Instruments Ltd.,

Cambridge, England) at 340 nm.

Serum Alkaline Phosphatase (SAP)

SAP was estimated using a Boehringer No. 123889 Alkaline Phosphatase (Colorimetric Method) Test-Combination. The enzyme activity was measured by the intensity of the colour formed in 30 min. at 37°C. The colour formed was read in a Cecil 292 Spectrophotometer at 405 nm.

Blood Urea

Blood samples for urea estimation were collected in plastic containers containing potassium oxalate as anti-coagulant and assayed by a modified urease-nesslerisation method of Archer and Robb (1925). A pure urea standard was used instead of ammonium salts. The results were obtained using an EEL Spectra 197 Colorimeter (Corning-EEL, Halstead, Essex) at 460 nm.

Blood Glucose

Blood was collected in plastic containers containing potassium oxalate and sodium fluoride to prevent glycolysis. After precipitation of protein with perchloric acid, glucose was estimated using a Boehringer Glucose (glucose oxidase/peroxidase) colorimetric method, No. 124028. The reaction time was reduced to 15 min. by incubating at 37°C. Readings were made within 16 min., using an EEL 197 Spectra Colorimeter at 600 nm.

Plasma Cortisol

Blood was collected in heparinised vacucontainers of sufficient volume to yield 2 ml. plasma. Plasma cortisol was measured using the fluorimetric method of Mattingly (1962). The fluorescence was measured using an EEL 244 Fluorimeter at 530 nm, tungsten lamp excitation wavelength 470 nm, emission wavelength 530 nm (Corning-EEL Ltd., Halstead, Essex).

T3 and T4

The serum for these estimations was stored at -20^{o}C immediately after separation. On the day of using the serum, samples were allowed to attain room temperature and were thoroughly agitated before radioimmunoassay using T3RIA (PEG) and T4RIA (PEG) commercial kits (Radiochemical Centre, Amersham, Bucks., England). The assays were done in duplicate. Very low values which could not be measured with confidence were repeated using a slight modification. Twice the volume of serum was used, and interference with T3 and T4 binding proteins was minimised by the use of additional blocking agent (thiomersalate) and the appropriate adjustment to the calculation made.

The standards supplied with the kits are of human source and the anti-serum is raised to human T3 and T4.

The counts were made on a Gamma-Guard 150 Counter (ICN Tracer Laboratory, U.K.), part of the Faculty facility in the Veterinary Biochemistry Unit, R(D)SVS. T3 values were

recorded in ng T3/ml. Conversion to SI units: ng T3/ml x 1.54 = nmol T3/l. T4 values were recorded in microgm T4/ 100ml. Conversion to SI units: microgm T4/100ml x 12.87 = nmol T4/l.

In some of the samples, excessive lipaemia was the cause of poor agreement of duplicates and in some cases it was not possible to assay T3 and T4.

DETERMINATION OF PROTEIN BOUND IODINE AND TOTAL IODINE

Although the problems associated with obtaining meaningful results from the assay of blood for its content of protein bound iodine (PBI) have been well recorded, and are discussed in the review of the literature, it was decided to undertake an investigation into the levels of PBI and total iodine (TI) in the different groups of dogs being studied.

Blood samples were obtained from a number of dogs in each of the groups. Every precaution was observed to avoid contamination of the sample with extraneous iodine. Serum samples were stored for up to 1 year at $-20^{o}C$ before being assayed.

From Groups N, HS, OH, P, A and EP the following numbers of dogs were used: 11, 17, 10, 22, 5 and 7, respectively, a total of 72. The identifying number of each dog which was blood sampled is given in Tables 60 , 61 , 62 , 63 , 64 and 65 .

Some dogs were blood sampled on more than one occasion for PBI and TI estimation.

The 17 dogs of Group HS were blood sampled before treatment for hypothyroidism and 16 of them were sampled after treatment had commenced.

INVESTIGATION OF SERUM CHOLESTEROL VALUES

Normal Dogs (Group N)

Serum cholesterol values were estimated on blood samples taken at the first examination of each of the 68 dogs in this group.

A series of experiments was undertaken to investigate the relationship of serum cholesterol levels to the time of feeding. The dogs, which were members of Group N, were housed separately in large cages in a room of constant temperature and given drinking water ad libitum. The diet consisted of 50% tinned proprietary meat ('Pal', 'Chum', 'Bounce', Pedigree Petfoods) and 50% biscuit ('Mick', Pedigree Petfoods, 'Winalot', Spillers) fed at approximately 30g per kg body weight, given as a single feed each day of the experiments.

Thirty two dogs were chosen on the basis of their availability for 5 experiments. Some dogs were used in more than one experiment.

Experiment 1

Seventeen normal dogs, numbers N10, 11, 12, 13, 14, 15, 21, 23, 26, 27, 28, 29, 30, 31, 32, 33 and 34 were used. The group was aged from 9 months to 7 years and weighed from 9.5 to 28 kg. It consisted of 3 each of Labradors, Greyhounds and terrier types, 2 each of Boxers and Collie crosses, and 1 each of Cairn, Labrador X, Poodle and Spaniel. There were 7 male, 1 male castrate, 8 female and 1 neutered

female. The dogs were fed daily at 2 p.m.

Blood samples were taken at 12 noon and 4 p.m. on the same day.

Experiment 2

Seven normal dogs, numbers N4, 8, 17, 19, 23, 36 and 68 were used. They were aged from 11 months to 8 years and weighed from 12.3 to 24 kg. The group consisted of 2 each of Greyhounds and Labradors and 1 each of Alsatian, Lurcher and terrier cross. There were 6 males and 1 female dog. The dogs were fed daily at 2 p.m.

Blood samples were taken immediately after feeding i.e. at 2.15 p.m., and at 4 p.m. on day 1, and 19 hours after feeding, i.e. at 9 a.m. on day 2.

Experiment 3

Seven normal dogs, numbers N5, 6, 15, 16, 17, 23 and 24 were used. The group was aged from 3 years to old and weighed from 10 to 28.5 kg. It consisted of 3 Greyhounds, 2 Collie crosses and 1 each of Irish Setter and terrier type. There were 3 male and 4 female dogs. On day 1, the dogs were fed, as usual, at 2 p.m. but on day 2 they were fed at 9.15 a.m. On day 1, blood samples were taken at 9 a.m., noon, 2.15 p.m. and 5 p.m. Samples were taken at 9 a.m., noon and 4 p.m. on day 2. These are referred to as samples 1 to 7 respectively.

Experiment 4

Four normal dogs, numbers N2, 3, 17 and 25 were used. They were aged from 4 months to 6 years. The dogs were 1 each of Border collie, Cairn, Greyhound and Retriever; all were male. The Cairn weighed 13.5 kg; the weights of the others were not recorded. The dogs were fed at 2 p.m. each day and blood sampled at 9 a.m., 11 a.m., 2.15 p.m. and 5 p.m. on day 1 and at 9 a.m., 11 a.m., 2.15 p.m. and 4 p.m. on day 2. These are referred to as samples 1 to 8 respectively.

Experiment 5

Six normal dogs, numbers N1, 15, 17, 20, 23 and 34 were used. They were aged from 3 years to old and weighed from 10 to over 23.5 kg. The dogs were 2 Greyhounds and 1 each of Alsatian, Boxer, Collie cross and terrier type. There were 3 male and 3 female dogs. The dogs were fed at 2 p.m. as usual on the day before sampling. On day 1 of sampling they were fed at 9 a.m. Five blood samples were taken on day 1 at 8.30 a.m., 11 a.m., 1 p.m., 3 p.m. and 5 p.m. and 1 sample at 9 a.m. on day 2, i.e. 24 hours after the last feed, a total of 6 samples.

These are referred to as samples 1 to 6 respectively.

Dogs with Suspected Hypothyroidism (Group HS)

Of the 47 dogs in Group HS, 12 had previously received thyroid therapy from other veterinary surgeons before they

entered the present investigation and 35 were previously untreated dogs. The former are referred to as HST and the latter as HSU cases. Before treatment was instituted in the present investigation, serum cholesterol assays were made on all of the dogs. In subgroup HSU, 4 dogs had 1 blood sample taken and 31 had more than one taken before treatment started. In subgroup HST, 4 dogs had 1 blood sample taken for cholesterol assay and 8 had more than 1 sample taken before the start of any treatment by the writer. The dates of sampling and the number of samples from each dog are listed in Tables 78 and 79 for the HSU and HST cases respectively.

Dogs with Other Hormonal Disorders (Group OH)

Blood samples were taken for serum cholesterol assay from each of the 47 dogs in this group at the time of their first clinical examination. In some cases, further samples were also assayed and for these cases the dates of sampling and the number of samples taken are listed in Table 81.

Dogs with Non-Hormonal Skin Diseases (Group NH)

Group NH consisted of three categories, 99 dogs with pyoderma (Group P), 57 with allergic skin conditions (Group A) and 49 with external parasitism (Group EP). Blood samples were taken for serum cholesterol estimation at the time of first clinical examination of 85, 24 and 43 dogs respectively, from the three groups. In some cases more

samples were taken later. For these cases the dates of sampling and the number of samples are listed in Tables 85 , 86 and 87 for Groups P, A and PE respectively.

ESTIMATION OF SERUM THYROXINE BY RADIOIMMUNOASSAY

Group N, Normal Dogs

Thyroxine (T4) values were estimated in the serum of the 62 dogs of Group N which were blood sampled at the time of their first examination. In some of the dogs, samples were taken later, for further assays.

Table 89 sets out the number of samples and the dates on which they were collected.

Thirty two dogs were chosen, on the basis of their availability, for a more detailed examination of T4 values in relation to the time of feeding. The 5 experiments have already been described in the section on the estimation of serum cholesterol. When blood samples were taken for cholesterol estimation, they were also taken for T4RIA.

Group HS, Dogs with Suspected Hypothyroidism

At the time of first examination of the dogs with suspected hypothyroidism, blood samples were taken for T4RIA. Subsequently, additional samples were taken from as many as possible but for some dogs only one sample was obtained and for one of the 47 dogs, no T4 assay was made. Some had more than one sample assayed before treatment started, in the case of the previously untreated dogs (HSU), or before it was resumed in the case of dogs that had been previously treated (HST). These groups consisted of 34 and 12 dogs sampled respectively. The dates of sampling and the number of samples taken are given in Table 100 .

Group OH, Dogs with Other Hormonal Disorders

T4RIA was conducted on serum from 41 dogs in this group, on samples taken at the time of first examination, and on a total of 47 subsequently. The dates of sampling and the number of samples are given in Table 101 .

Group P, Dogs with Pyoderma

T4RIA was conducted on 77 dogs in this group. The dates of sampling and the number of samples are given in Table 102 . Some dogs were sampled more than once.

Group A, Dogs with Allergic Conditions

T4RIA was conducted on blood samples from 45 dogs of this group. The assay was made on more than one sample in some cases. The dates of sampling and number of samples are given in Table 103 .

Group PE, Dogs with External Parasitism

At the time of their being first examined, blood samples were taken from 36 dogs and T4RIA conducted on them. The dates and numbers of samples are presented in Table 104. Some dogs were sampled more than once.

ESTIMATION OF SERUM TRIIODOTHYRONINE BY RADIOIMMUNOASSAY

Radioimmunoassay of triiodothyronine was undertaken on the blood samples which had been collected for T4RIA. This involved the dogs of Group N generally, the members of Group N in the 5 experiments investigating the relationship of cholesterol at T4 levels to intervals since feeding, and the samples taken from the dogs of Groups HS, OH, P, A and EP. Because the arrangements were the same for the T3 as for the T4 assays it is not proposed to repeat them.

ESTIMATION OF SOME SERUM ENZYMES AND OTHER BLOOD CONSTITUENTS

Some degree of liver damage has been associated with hypothyroidism. Estimations were made of SGOT, SGPT and SAP in a number of the dogs in each group, as liver damage is among the conditions known to increase the amount of these enzymes in the circulation. Assays were also undertaken of plasma cortisol, blood urea and blood glucose in some cases. More than 1 sample was assayed in some cases. The numbers of dogs on which the tests were conducted, in each group, are given in Table 113.

In view of the results, it was considered unnecessary to tabulate the dogs individually except in the case of those which had the adrenocorticotrophic hormone (ACTH) stimulation test applied. The test is conducted when further information about adrenal cortical function is required. In dogs with hyperadrenalcorticalism (canine Cushing's disease), an injection of ACTH results in a considerable increase in plasma cortisol levels, whereas in normal dogs the effect of the injection is to raise the level to not more than about twice the pre-injection level. The test was conducted as follows. After a blood sample had been taken, tetracosactrim acetate BP (Synacthen, Ciba Ltd.), a synthetic substance with ACTH activity, was injected intra-muscularly in amounts of 0.1 mg or 0.2 mg for dogs under or over 9 kg body weight, respectively. A blood sample was taken 30 min. later and if further samples were required, they also were taken at

30 min. intervals. The cortisol concentration of the plasma of the blood samples was then ascertained.

HAEMATOLOGICAL INVESTIGATIONS

Introduction

Reference has been made to the occurrence of normocytic, normochromic anaemia, usually at the sub-clinical level, in cases of hypothyroidism. This was investigated to ascertain its frequency and to compare the situation in the different groups of dogs being studied.

Normal Dogs (Group N)

From the group of 68 normal dogs, blood samples were taken once from 49 dogs.

Cases of Suspected Hypothyroidism (Group HS)

Blood samples were taken from 45 of the 47 dogs in the group.

Some of the dogs had been previously treated by colleagues. On this basis, the 45 dogs were divided into a sub-group of 33 which had not previously received thyroid therapy (suspected hypothyroid cases untreated or HSU) and another sub-group of 12 dogs reported to have been previously treated with thyroid (suspected hypothyroid cases treated or HST).

In 11 cases one sample was obtained before treatment was begun by the present writer and further samples were not obtained. In 34 dogs, as well as obtaining such pre-treatment samples, from one to 14 samples were obtained post-treatment.

Dogs with 'Other Hormonal' Conditions (Group OH)

Blood samples were taken once from 44 of the 47 dogs in this category.

Dogs with Non-Hormonal Skin Conditions (Group NH)

This group consisted of 205 dogs of which 99 had pyoderma, 57 had allergic conditions and 49 had ecto-parasitic infestations. Blood samples were taken on one occasion from 80,54 and 35 respectively of these dogs, a total of 169.

Blood samples

Depending on the size of the dog, blood samples were taken from either the cephalic, recurrent tarsal or jugular vein, using minimal restraint to lessen the likelihood of excitement. The vein was engorged by digital pressure and the blood was withdrawn using sterile disposable needles and plastic syringes. The blood was immediately placed in plastic containers in which coagulation was prevented by the presence of di-potassium ethylene-diamine-tetra-acetic acid (EDTA; sequestrene).

Red Cell Counts

Red cell counts were made on a ZF6 Coulter electronic counter (Coulter Electronics Ltd., Harpenden, Herts.). Three counts were made of each sample and the mean taken. The number of RBC was recorded in 10^{12}/per litre (10^{12}/l).

Packed Cell Volume (PCV; Haematocrit)

Blood samples were centrifuged for 5 minutes at 12,000 G in a Hawksley Microhaematocrit Centrifuge (Hawksley Ltd., Lancing, England). The tubes were read in the Micro-Haematocrit Reader and results recorded as litres of packed cells per litre of whole blood (l/l).

Haemaglobin (Hb)

The cyamethaemoglobin method (Coulter Electronics Instruction Manual) using a Coulter Haemaglobinometer was employed. All haemoglobin measurements were performed on the day the blood was collected and the results recorded in g/dl.

Mean Corpuscular Volume (MCV)

This is an erythrocyte index referring to the average or mean size in microns of the red blood cells and it is obtained by calculation:

$$MCV = \frac{PCV}{\text{Red cell count } (10^{12}/l)}$$

The answer is expressed in femto-Litres (fl).

Mean Corpuscular Haemoglobin Concentration (MCHC)

This index indicates the mean Hb concentration per RBC. It is obtained by calculation:

$$MCHC = \frac{Hb\,(g/dl)}{PCV\ (l/l)}$$

The answer is expressed in g/dl.

Mean Corpuscular Haemoglobin (MCH)

MCH is an expression of the mean Hb content of a single RBC. It is obtained by calculation:

$$MCH = \frac{Hb\,(g/dl) \times 10}{RBC\ (10^{12}/l)}$$

The answer is expressed in pico-grammes (pg).

White Cell Counts

Total leucocyte counts were carried out on a ZF6 Coulter electronic counter, the mean of 3 counts being taken for each sample. The numbers are recorded as 10^9 per litre ($10^9/l$).

Differential white cell counts were made on smears of blood prepared immediately after obtaining the blood sample. The smears were stained with Leishman's stain. Under the microscope, a minimum of 200 cells was counted and differentiated for each blood sample, using the 4-field meander method (Dacie & Lewis, 1975).

RESULTS

CLINICAL OBSERVATIONS

Results

Not all of the cases in the different groups could be followed up because of the failure of some clients to continue with regular visits to the Clinic with their dogs. Sometimes this was because either the case had died or started to improve, or the owner did not wish to continue with treatment. Some had moved to other districts.

Group HS

The 47 cases which on clinical grounds were diagnosed as suspected hypothyroidism showed a variety of clinical signs. The observations made on each dog are recorded in Table 24 in which signs generally referable to a particular system of the body are placed together. The frequency of occurrence of each of the clinical signs in the group is presented in Table 25 .

Information about the presence or absence of alopecia and its distribution when present is given in Table 26 . The results of bacteriological examination of the skin in those dogs which appeared clinically to have a secondary infection of the skin are given in Table 27 . *Staphylococcus aureus* predominated.

Microscopical examination of prepared skin scrapings failed to reveal the presence of external parasites in 46 dogs. Only one dog, HS27, had one demodectic mite present in the first preparation; further scrapings were negative.

TABLE 24 Group HS, Clinical Signs Present in Dogs with Suspected Hypothyroidism

Dog No.	HS 1	HS 2	HS 3	HS 4	HS 5	HS 6	HS 7	HS 8	HS 9	HS 10	HS 11	HS 12	HS 13	HS 14	HS 15	HS 16	HS 17	HS 18	HS 19	HS 20	HS 21	HS 22	HS 23	HS 24	HS 25	HS 26	HS 27	HS 28
1. Skin																												
Cold Skin							+			+	+												+					+
Comedones													+					+										
Conjunctivitis		+																										
Erythema								+														+		+				
Hyperelasticity											+																	
Hyperkeratosis							+														+							
Hyperpigmentation		+	+	+	+				+		+				+						+	+		+	+		+	
Lichenified		+							+												+							
Otitis Externa		+									+		+								+							
Puffy Face																					+							
Pruritus		+						+						+								+			+	+		
Scaliness																							+				+	
Seborrhoea									+																			
Skin Inflamed	+	+		+				+	+		+		+	+	+	+	+	+		+	+	+	+	+	+	+		
Thick Skin		+						+			+							+			+		+					
Thin Skin									+	+																		
Wet Eczema																												

TABLE 24 (continued)

Dog No.	HS 29	HS 30	HS 31	HS 32	HS 33	HS 34	HS 35	HS 36	HS 37	HS 38	HS 39	HS 40	HS 41	HS 42	HS 43	HS 44	HS 45	HS 46	HS 47
1. Skin																			
Cold Skin																			
Comedones																			
Conjunctivitis	+																		
Erythema					+					+									
Hyperelasticity																			
Hyperkeratosis																			
Hyperpigmentation	+		+		+		+				+			+			+		
Lichenified			+																
Otitis Externa	+		+		+		+												
Puffy Face																			
Pruritus			+		+					+							+		
Scaliness																			
Seborrhoea																		+	+
Skin Inflamed	+	+	+		+	+	+		+	+	+	+							
Thick Skin	+		+		+		+												
Thin Skin																			
Wet Eczema																			

TABLE 24 (continued)

Dog No.	HS 1	HS 2	HS 3	HS 4	HS 5	HS 6	HS 7	HS 8	HS 9	HS 10	HS 11	HS 12	HS 13	HS 14	HS 15	HS 16	HS 17	HS 18	HS 19	HS 20	HS 21	HS 22	HS 23	HS 24	HS 25	HS 26	HS 27	HS 28
2. Hair																												
Alopecia																												
i) Symmetrical	+	+	+				+		+				+	+	+	+	+			+	+	+	+				+	+
ii) Asymmetrical				+	+	+		+		+	+							+	+						+	+		
Dry, sparse, rough		+				+		+	+	+	+							+									+	+
Easily Epilated		+								+																		+
3. Behaviour																												
Lethargy	+	+	+		+	+	+		+	+	+		+	+			+	+	+	+	+	+	+	+			+	+
Nervousness				+																								
Sleepiness		+				+													+		+			+				+
Thermophilia									+	+			+								+		+					+
4. Bodily Condition																												
Weight Gained	+		+	+	+	+	+	+	+		+		+	+	+		+		+		+		+	+	+			+
Weight Lost																				+								
5. Digestive																												
Anorexia						+																						+
Constipation						+																						
Diarrhoea															+			+										
Polyphagia									+				+								+							
Pot Belly																												
Vomiting																												+

TABLE 24 (continued)

Dog No.	HS 29	HS 30	HS 31	HS 32	HS 33	HS 34	HS 35	HS 36	HS 37	HS 38	HS 39	HS 40	HS 41	HS 42	HS 43	HS 44	HS 45	HS 46	HS 47
2. Hair																			
Alopecia																			
i) Symmetrical					+		+					+	+	+					
ii) Asymmetrical	+			+				+			+					+	+	+	+
Dry, sparse, rough				+			+				+	+					+	+	+
Easily Epilated				+															
3. Behaviour																			
Lethargy	+		+	+	+	+	+	+			+	+	+	+		+	+	+	
Nervousness							+												
Sleepiness		+															+		
Thermophilia																			
4. Bodily Condition																			
Weight Gained	+	+	+	+	+	+	+		+	+	+	+	+	+		+	+	+	+
Weight Lost																			
5. Digestive																			
Anorexia		+																	
Constipation																			
Diarrhoea											+								
Polyphagia				+												+	+	+	+
Pot Belly										+	+								
Vomiting											+								

TABLE 24 (continued)

Dog No.	HS 1	HS 2	HS 3	HS 4	HS 5	HS 6	HS 7	HS 8	HS 9	HS 10	HS 11	HS 12	HS 13	HS 14	HS 15	HS 16	HS 17	HS 18	HS 19	HS 20	HS 21	HS 22	HS 23	HS 24	HS 25	HS 26	HS 27	HS 28
6. Urogenital																												
Balanitis																												
Cystitis																												
False Pregnancy																	+								+			
Gynecomastia																				+							+	
Polydipsia																	+				+							
Polyuria																												
7. Circulatory																												
Cardiac Condition																		+										
Pale Mucosa																												
Tachycardia																												
Weak Pulse								+										+			+							
8. Respiratory																												
Breathlessness																												
Cough																		+										+
9. Other Conditions																												
Anal Sacs Impacted		+															+											
Liver Enlarged																												
Lymph Nodes Enlarged		+								+			+								+							

TABLE 24 (continued)

Dog No.	HS 29	HS 30	HS 31	HS 32	HS 33	HS 34	HS 35	HS 36	HS 37	HS 38	HS 39	HS 40	HS 41	HS 42	HS 43	HS 44	HS 45	HS 46	HS 47
6. Urogenital																			
Balanitis		+																	
Cystitis		+																	
False Pregnancy					+														
Gynecomastia																			
Polydipsia		+															+	+	
Polyuria		+															+	+	
7. Circulatory																			
Cardiac Condition																			
Pale Mucosa																+	+		
Tachycardia																			
Weak Pulse											+								
8. Respiratory																			
Breathlessness																		+	
Cough																			
9. Other Conditions																			
Anal Sacs Impacted					+														
Liver Enlarged											+								
Lymph Nodes Enlarged											+								

TABLE 25 Group HS, Summary of Clinical Signs in Dogs with Suspected Hypothyroidism

Clinical Sign	No. of Dogs	Per-cen-tage	Clinical Sign	No. of Dogs	Per-cen-tage
Alopecia	39	83.0	Cough	2	4.3
i) Symmetrical	21	44.7	Gynecomastia	2	4.3
ii) Asymmetrical	18	38.3	Hyperkeratosis	2	4.3
Lethargy	36	76.6	Nervousness	2	4.3
Skin Inflamed	29	61.7	Pale Mucosa	2	4.3
Hyperpigmentation	19	40.4	Pot Belly	2	4.3
Dry, sparse, rough coat	16	34.0	Scaliness	2	4.3
Pruritus	10	21.3	Thin Skin	2	4.3
Thick Skin	10	21.3	Vomiting	2	4.3
Otitis Externa	8	17.0	Balanitis	1	2.1
Polyphagia	8	17.0	Breathlessness	1	2.1
Sleepiness	8	17.0	Cardiac Condition	1	2.1
Thermophilia	6	12.8	Constipation	1	2.1
Cold Skin	5	10.6	Cystitis	1	2.1
Erythema	5	10.6	Enlarged Liver	1	2.1
Lymph Node Enlarged	5	10.6	Hyperelasticity Skin	1	2.1
Polydipsia	5	10.6	Puffy Face	1	2.1
Easily Epilated	4	8.5	Weight Loss	1	2.1
Lichenified	4	8.5			
Weak Pulse	4	8.5			
Anorexia	3	6.4			
Anal Sac Impacted	3	6.4			
Diarrhoea	3	6.4			
False Pregnancy	3	6.4			
Polyuria	3	6.4			
Seborrhoea	3	6.4			
Comedones	2	4.3			
Conjunctivitis	2	4.3			

TABLE 26 Group HS, Distribution of Alopecia in cases of Suspected Hypothyroidism

Dog No.	HS 1	HS 2	HS 3	HS 4	HS 5	HS 6	HS 7	HS 8	HS 9	HS 10	HS 11	HS 12	HS 13	HS 14	HS 15	HS 16
Treated before first examination										+		+	+		+	
Alopecia																
Symmetrical	+	+	+				+		+				+	+	+	+
Asymmetrical				+	+	+		+		+	+					
Patches	+	+	+	+	+	+	+	+	+	+			+	+		+
Sparse Coat		+				+		+	+	+	+			+		
Site Affected																
Face																
Head							+									
Ear							+									
Neck							+									
Withers		+								+						
Dorsum								+	+				+	+		
Lumbar		+	+											+		
Lumbo-Sacral		+												+		
Flank	+	+		+	+	+	+		+				+	+	+	+
Hip		+														
Posterior Hip		+														
Tail Head		+					+									
Tail																
Lateral Chest		+		+												
Sternum							+									
Axilla																
Groin				+												
Belly		+					+		+					+		
Fore Leg																
Hind Leg		+														
Thigh		+					+									
Period to first sign of recovery, (days)		24	30	21	45	60	30	21	30	60	39		10	77		
Response to first treatment		±	+	+	+	+	+	+	±	±	+	-	+	+	?	?

TABLE 26 (continued)

Dog No.	HS 17	HS 18	HS 19	HS 20	HS 21	HS 22	HS 23	HS 24	HS 25	HS 26	HS 27	HS 28	HS 29	HS 30	HS 31	HS 32
Treated before first examination	+		+												+	
Alopecia																
Symmetrical	+			+	+	+	+				+	+				
Asymmetrical		+	+						+	+			+			+
Patches			+													
Sparse Coat		+									+	+				
Site Affected																
Face										+						
Head																
Ear																
Neck							+									
Withers																+
Dorsum																
Lumbar									+							
Lumbo-Sacral	+			+					+							
Flank		+	+				+				+	+				
Hip																
Posterior Hip																
Tail Head																
Tail																
Lateral Chest	+			+			+				+	+				+
Sternum												+				+
Axilla																
Groin																
Belly											+					+
Fore Leg																
Hind Leg							+									
Thigh		+	+				+									
Period to first sign of recovery, (days)			60			7	50	50	18	10	7		7	30		
Response to first treatment	?	±	+	?	?	+	+	+	+	+	+	?	+	+	?	+

TABLE 26 (continued)

Dog No.	HS 33	HS 34	HS 35	HS 36	HS 37	HS 38	HS 39	HS 40	HS 41	HS 42	HS 43	HS 44	HS 45	HS 46	HS 47
Treated before first examination			+		+					+				+	+
Alopecia															
Symmetrical	+		+					+	+	+					
Asymmetrical				+			+					+	+	+	+
Patches			+	+			+			+					
Sparse Coat	+		+				+						+		+
Site Affected															
Face															
Head															
Ear															
Neck								+							
Withers															
Dorsum	+						+					+	+		
Lumbar															
Lumbo-Sacral			+	+			+						+		
Flank								+	+	+					
Hip															
Posterior Hip			+				+	+							
Tail Head															
Tail								+		+					
Lateral Chest								+							
Sternum								+							
Axilla															
Groin															
Belly															
Fore Leg															
Hind Leg							+								
Thigh								+							
Period to first sign of recovery, (days)	14					60	30								
Response to first treatment	+	?				+	+	?	+	?	?	+	?	?	

Response to first treatment: + = continued to benefit
± = early favourable response not maintained
? = outcome unknown
- = dog did not benefit

Period to first recovery: the first sign of recovery was not necessarily in respect of the skin, it was often behavioural.

TABLE 27 Group HS: Organism cultured from the skin of selected cases of suspected hypothyroidism

Dog No.	Organism	Times isolated	Duration of Hypothyroidism	Pruritus
HS2	Staph aureus	6	3 years	+
HS8	Staph aureus	2	2 months	+
HS11	Staph aureus	2	3 months	+
HS13	Staph aureus	1	4 years	-
HS20	Staph aureus	1	7 months	-
HS23	Staph aureus	1	?	-
HS25	Staph aureus	1	1 year	+
HS30	Staph aureus	1	?	+
HS31	Staph aureus, streptococci, diphtheroids	3 2 1	3 months	-
HS33	Staph aureus	2	3 years	+
HS34	Staph aureus	1	2 years	+
HS35	Staph aureus, staph epidermidis	1	1 year	-

Group OH

The diagnosis ascribed to the 47 cases considered to be due to hormonal disorders other than of thyroid origin are shown in Table 28 . Where a diagnosis was not made, the main presenting signs are given.

The details of the clinical findings are given for each dog in Table 29 and these are summarised in Table 30. The results of the bateriological examinations which were conducted on 7 of these dogs are presented in Table 31. Staphylococcus aureus predominated.

Group NH
Group NHP

The clinical signs and bacteriological findings of the dogs affected with pyoderma are presented in Table 32 . The frequency of occurrence of each clinical sign in the group is given in Table 33. . Not all cases were subjected to bacteriological examination but 54 were. Of these, 6 gave negative results on culture and in 26 Staph. aureus only was isolated. It was present with other infections in 14 cases.

Group NHA

The clinical signs in the dogs with allergic skin conditions are set out in Table 34 and summarised in Table 35. Cultural examination of the skin of 11 of the dogs

resulted in the isolation of Staph. aureus from 10 cases and one case was negative on culture. The positive cases were A3, A4, A7, A8, A9, A12, A30, A31, A34 and A41. The negative case was A55.

Group NHEP

The clinical sign in the dogs affected with external parasitism are presented in Table 36 and summarised in Table 37. Five cases were subjected to culture for skin infections. Two were positive for Staph. aureus (EP1, EP4) and one case had Staph. aureus plus beta-haemolytic (EP29) streptococci. Two cases were negative (EP6, EP38).

TABLE 28

Group OH, Diagnosis or Salient Feature Ascribed to Cases of "Other Hormonal" Disease

No. of Dog	Diagnosis	No. of Dog	Diagnosis
OH1	Sertoli Cell Tumour (S.C.T.)	OH27	Hair loss
OH2	S.C.T.	OH28	Cushings-like syndrome
OH3	S.C.T.	OH29	Hair loss
OH4	S.C.T.	OH30	Hair loss
OH5	S.C.T.	OH31	Hair loss, Otitis
OH6	S.C.T.	OH32	Acanthosis, Pyoderma
OH7	S.C.T.	OH33	Alopecia
OH8	Iatrogenic Cushings	OH34	Seborrhoea, Wet Excema
OH9	Cushings-like syndrome	OH35	Alopecia
OH10	" " "	OH36	Alopecia
OH11	Iatrogenic Cushings	OH37	Lethargic and over-weight
OH12	Cushings-like syndrome	OH38	Alopecia
OH13	Iatrogenic Cushings	OH39	Seborrhoea
OH14	" " " "	OH40	Alopecia
OH15	Hormonal Alopecia	OH41	Seborrhoea
OH16	Alopecia & Dermatitis	OH42	Hair loss, locally hyperpigmented
OH17	Hormonal Alopecia & Dermatitis	OH43	Hormonal Alopecia
OH18	Alopecia, overweight & Dermatitis	OH44	Hair loss, Lethargy, Weight gain
OH19	Hair loss & Acanthosis	OH45	Cushings-like syndrome
OH20	Hair loss & False Pregnancy	OH46	Hormonal Alopecia
OH21	Hormonal Alopecia	OH47	Cushings-like syndrome
OH22	Seborrhoea & Alopecia		
OH23	Iatrogenic Cushings		
OH24	Hormonal Alopecia		
OH25	Alopecia & Seborr-hoea		
OH26	Alopecia		

TABLE 29 Group OH, Clinical Signs Present in Dogs with Other Hormonal Conditions

Dog No.	OH 1	OH 2	OH 3	OH 4	OH 5	OH 6	OH 7	OH 8	OH 9	OH 10	OH 11	OH 12	OH 13	OH 14	OH 15	OH 16	OH 17	OH 18	OH 19	OH 20	OH 21	OH 22	OH 23	OH 24	OH 25	OH 26	OH 27	OH 28
1. Skin																												
Acanthosis																	+		+									
Biting/Pulling hair																+	+			+								
Calcinosis Cutis								+			+																	
Cold Skin																												
Comedones												+																
Erythema								+									+	+									+	
Excoriations												+					+	+										
Fibroma					+																							
Hyperpigmentation	+					+			+						+	+		+	+			+						
Lichenified									+																			
Loss of Elasticity												+																
Macules	+																											
Otitis Externa		+						+										+				+						
Pruritus			+					+	+		+			+		+	+	+		+	+	+	+			+		
Scaliness										+										+					+		+	
Seborrhoea	+																					+			+			
Skin Inflamed								+	+		+		+	+	+	+	+	+		+		+	+		+			
Thick Skin								+	+								+									+	+	
Thin Skin																							+		+			
Warts																												+
Wet Eczema																												

TABLE 29 (continued)

Dog No.	OH 29	OH 30	OH 31	OH 32	OH 33	OH 34	OH 35	OH 36	OH 37	OH 38	OH 39	OH 40	OH 41	OH 42	OH 43	OH 44	OH 45	OH 46	OH 47
1. Skin																			
Acanthosis														+					
Biting/pulling hair			+	+															
Calcinosis Cutis																			
Cold Skin		+																	
Comedones																			
Erythema			+		+	+								+					
Excoriations	+																		
Fibroma																			
Hyperpigmentation	+		+				+					+							+
Lichenified																			
Loss of Elasticity																			
Macules						+													+
Otitis Externa																			
Pruritus	+		+	+		+									+				
Scaliness			+			+					+					+			
Seborrhoea						+					+		+						
Secondary Infection	+													+	+				+
Thick Skin	+	+	+										+	+				+	
Thin Skin																			
Warts																			
Wet Eczema						+													

TABLE 29 (continued)

Dog No.	OH 1	OH 2	OH 3	OH 4	OH 5	OH 6	OH 7	OH 8	OH 9	OH 10	OH 11	OH 12	OH 13	OH 14	OH 15	OH 16	OH 17	OH 18	OH 19	OH 20	OH 21	OH 22	OH 23	OH 24	OH 25	OH 26	OH 27	OH 28
2. Hair																												
Alopecia																												
i) Symmetrical	+						+			+		+			+			+		+	+	+					
ii) Asymmetrical			+					+	+					+		+								+		+	+	+
Dry, sparse, rough	+							+				+			+			+		+		+				+		+
Easily Epilated		+						+	+						+		+			+								
Excess Moult		+																	+		+						+	
3. Behaviour																												
Lethargy									+		+						+								+			
Nervousness																	+							+				
Sleepiness												+					+	+										
Thermophilia																	+											
4. Bodily Condition																												
Weight Gained		+	+		+			+	+	+	+											+		+				
Weight Lost															+													
5. Digestive																												
Anorexia																									+			
Diarrhoea																					+				+			
Polyphagia										+					+		+	+	+		+							+
Pot Belly								+		+														+				+

TABLE 29 (continued)

Dog No.	OH 29	OH 30	OH 31	OH 32	OH 33	OH 34	OH 35	OH 36	OH 37	OH 38	OH 39	OH 40	OH 41	OH 42	OH 43	OH 44	OH 45	OH 46	OH 47
2. Hair																			
Alopecia																			
i) Symmetrical							+								+				
ii) Asymmetrical					+			+		+		+				+		+	
Dry, sparse, rough		+								+		+				+			
Easily Epilated																			
Excess Moult	+	+	+	+			+	+						+		+	+		
3. Behaviour																			
Lethargy	+								+										+
Nervousness																			
Sleepiness	+	+																	
Thermophilia	+																		
4. Bodily Condition																			
Weight Gained	+		+	+			+		+	+				+					
Weight Lost		+																	
5. Digestive																			
Anorexia	+																		
Diarrhoea																			
Polyphagia																			
Pot Belly																			+

TABLE 29 (continued)

Dog No.	OH 1	OH 2	OH 3	OH 4	OH 5	OH 6	OH 7	OH 8	OH 9	OH 10	OH 11	OH 12	OH 13	OH 14	OH 15	OH 16	OH 17	OH 18	OH 19	OH 20	OH 21	OH 22	OH 23	OH 24	OH 25	OH 26	OH 27	OH 28
6. Urogenital																												
False Pregnancy									+								+			+		+						
Gynecomastia		+							+													+						
Polydipsia										+																		+
Polyuria										+																		+
Prepuce Pendulous						+																						
Prostate Enlarged	+					+	+																					
Testicle Abnormal			+		+																							
Urine Dribbling	+																											
Urine Purulent	+																											
7. Circulatory																												
Pale Mucosa							+																					
Tachycardia																												
6. Respiratory																												
Bilateral Nasal Discharge			+																									
Breathlessness																								+				
Cough																												
9. Other Conditions																												
Anal Sacs Impacted																		+		+	+			+			+	+
Lymph Nodes Enlarged								+	+								+	+								+		+

TABLE 29 (continued)

Dog No.	OH 29	OH 30	OH 31	OH 32	OH 33	OH 34	OH 35	OH 36	OH 37	OH 38	OH 39	OH 40	OH 41	OH 42	OH 43	OH 44	OH 45	OH 46	OH 47
6. Urogenital																			
False Pregnancy	+																		
Gynecomastia	+															+			
Polydipsia								+											+
Polyuria																			+
Prepuce Pendulous																			
Prostate Enlarged																			
Testicle Abnormal																	+	+	
Urine Dribbling																			
Urine Purulent																			
7. Circulatory																			
Pale Mucosa																			
Tachycardia									+										
8. Respiratory																			
Bilateral Nasal Discharge																			
Breathlessness																			
Cough			+																
9. Other Conditions																			
Anal Sacs Impacted																+	+		
Lymph Nodes Enlarged																			

TABLE 30

Group OH. Summary of Clinical Signs in dogs with "Other Hormonal" conditions.

Clinical Sign	No. of Dogs	Per-centage	Clinical Sign	No. of Dogs	Per-centage
Alopecia	26	55.3	Prostate enlarged	3	6.4
i) symmetrical	11	23.4	Polyuria	3	6.4
ii) asymmetrical	15	31.9	Anorexia	2	4.3
Pruritus	18	38.3	Calcinosis cutis	2	4.3
Skin inflammation	17	36.2	Cold skin	2	4.3
Dry, sparse, rough coat	13	27.7	Diarrhoea	2	4.3
Excess moult	13	27.7	Nervousness	2	4.3
Hyperpigmentation	13	27.7	Thermophilia	2	5.3
Thick skin	11	23.4	Thin skin	2	4.3
Erythema	9	19.2	Weight lost	2	4.3
Anal Sacs Impacted	8	17.0	Bilateral nasal discharge	1	2.1
Scaliness	8	17.0	Breathlessness	1	2.1
Lethargy	7	14.9	Cough	1	2.1
Polyphagia	7	14.9	Comedones	1	2.1
Biting/pulling hair	6	12.8	Fibroma	1	2.1
Easily epilated	6	12.8	Lichenified	1	2.1
Lymph nodes enlarged	6	12.8	Loss of skin elasticity	1	2.1
Seborrhoea	6	12.8	Pale mucosa	1	2.1
False pregnancy	5	10.6	Prepuce Pendulous	1	2.1
Gynocomastia	5	10.6	Tachycardia	1	2.1
Pot belly	5	10.6	Urine purulent	1	2.1
Sleepiness	5	10.6	Warts	1	2.1
Otitis externa	4	8.5	Wet eczema	1	2.1
Polydipsia	4	8.5			
Testicle abnormal	4	8.5			
Acanthosis	3	6.4			
Excoriations	3	6.4			
Macules	3	6.4			

TABLE 31

Group OH: organisms cultured from the skin of selected "other hormonal" cases

Dog No.	Organism	Times isolated	Duration of disorder	Pruritus
OH3	Pasteurella multocida predominatea	1	2 years	+
OH8	Staph. aureus	3	1 year	+
OH9	Staph. aureus beta haemolytic gpG streptococci	1	4 years	+
OH11	Staph. aureus	1	3 years	+
OH17	Staph. aureus	2	4 years	+
OH22	Staph. aureus	1	1 year	+
OH31	Beta-haemolytic gpG streptococci, Staph. aureus	1	1 year	+

Table 32

Group NHP Clinical and microbiological findings in dogs with pyoderma

Dog No.	Dermatitis										Skin and Coat										Other Clinical Signs										Weight	Microbiological findings
	Chronic	Acute	Severe	Mild	Generalised	Localised	Otitis	Interdigital	Pruritus		Alopecia	Easily epilated	Excess moult	Thick skin	Thin skin	Scaliness	Seborrhoea	Erythema	Hyperkeratosis	Hyper-pigmentation	Acanthosis	Anal sacs impacted	Lymph nodes enlarged	Pregnancy False	Anorexia	Polyphagia	Polydipsia	Lethargy, easily tired	Sleepiness	Thermophilia	Overweight or weight gain	
P1	+			+		+			+			+		+				+														occasional bacterial colonies with little significance
P2		+		+		+			+				+						+	+												Staph. aureus
P3	+		+		+		+		+					+				+		+												Staph. aureus, yeasts of pityroporum
P4	+		+			+	+	+	+					+													+		+	+		Staph. epidermidis Staph. aureus
P5	+			+		+			+				+			+					+											negative
P6	+			+		+										+												+	+			Staph. aureus, beta-haem Group G strep.
P7	+		+		+		+													+			+				+				+	Staph. aureus and beta-haem group G strep
P8		+		+		+		+			+		+																			
P9		+		+		+			+																							
P10		+		+		+			+				+																			
P11		+		+		+		+	+				+					+												+	yeasts of unknown nature Alpha-haem strep & occ. colonies of diptheroids
P12		+		+		+			+									+												+	Coagulase +ve Staph. aur.
P13		+		+		+			+		+		+	+				+												+	Staph. aureus
P14		+		+		+			+									+												+	
P15	+			+		+																										
P16	+			+		+							+																			
P17		+		+		+			+																						+	Staph. aureus
P18	+		+			+		+											+	+											+	Staph. aureus beta-haem Group G strep.

Table 32 (contd.)

		Microbiological findings	P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34	P35	P36	P37	P38	P39	P40	P41
Weight	Overweight or weight gain			+	+		+	+								+			+					+
Other clinical signs	Thermophilia							+																	
	Sleepiness							+																	
	Lethargy, easily tired						+	+																	+
	Polydipsia																								
	Polyphagia																								
	Anorexia																								
	False pregnancy																								
	Lymph nodes enlarged							+																	
	Anal sacs impacted																								
Skin and Coat	Acanthosis																								
	Hyper-pigmentation			+				+				+		+				+					+	+	
	Hyperkeratosis																								
	Erythema										+				+			+			+			+	
	Seborrhoea																								
	Scaliness				+																			+	
	Thin skin						+																		
	Thick skin																						+		
	Excess moult				+							+					+		+					+	
	Easily epilated				+							+													
	Alopecia																								
Dermatitis	Pruritus			+		+	+	+					+	+	+	+		+	+			+		+	
	Interdigital										+						+			+					
	Otitis			+	+			+			+			+	+						+				
	Localised		+		+	+	+						+				+	+	+	+	+	+	+		+
	Generalised			+				+	+	+	+	+		+	+	+								+	
	Mild		+	+	+	+	+	+			+		+	+	+					+	+	+	+		+
	Severe		•						+	+		+				+	+	+	+					+	
	Acute													+						+	+	+	+		
	Chronic		+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+					+	+
	Dog No.		P19	P20	P21	P22	P23	P24	P25	P26	P27	P28	P29	P30	P31	P32	P33	P34	P35	P36	P37	P38	P39	P40	P41

Microbiological findings:
- P19: Staph. aureus
- P20: Staph. aureus
- P21: Staph. aureus
- P22: Staph. aureus
- P23: Staph. aureus
- P24: Staph. aureus, beta-haem. Group G Strep.
- P25–P26: (blank)
- P27: Staph. aureus
- P28: negative
- P29–P30: (blank)
- P31: Staph. aureus
- P32: (blank)
- P33: Staph. aureus, beta-haem. Group G Strep.
- P34: Staph. aureus
- P35: Staph. aureus
- P36: Unidentified gram -ve coccobacillus and Staph. aureus
- P37: (blank)
- P38: Staph aureus
- P39–P41: (blank)

Table 32 (contd.)

		Dog No.	P42	P43	P44	P45	P46	P47	P48	P49	P50	P51	P52	P53	P54	P55	P56	P57	P58	P59	P60
		Microbiological findings	Staph. aureus, beta-haem. Group G streptococci	Staph. aureus	Staph. aureus	Staph. aureus	Staph. aureus	Staph. aureus	Staph. aureus		Staph. aureus	Staph. aureus	negative	Staph. aureus	Staph. epidermidis, alpha haem. strep. organism resembling Neisseria.	Staph. aureus			Staph. aureus, beta-haem Group G streptococci	Staph. aureus Genus Proteus (ear)	
Weight		Overweight or weight gain		+							+			+			+	+	+	+	
Other Clinical Signs		Thermophilia																			
		Sleepiness																			+
		Lethargy, easily tired																			+
		Polydipsia																+			
		Polyphagia											+					+			
		Anorexia																			
		False pregnancy																		+	
		Lymph nodes enlarged																			
		Anal sacs impacted																		+	
Skin and Coat		Acanthosis																	+		+
		Hyper-pigmentation										+					+		+		
		Hyperkeratosis																	+		
		Erythema										+			+	+					
		Seborrhoea									+										
		Scaliness												+							
		Thin Skin																			
		Thick Skin	+																+		+
		Excess moult		+				+				+			+				+	+	+
		Easily epilated																	+		
		Alopacia									+	+									
Dermatitis		Pruritus		+		+		+			+	+		+		+	+		+	+	
		Interdigital		+														+	+		
		Otitis	+								+	+							+		+
		Localised	+	+	+		+	+		+				+		+					+
		Generalised				+			+		+	+	+		+		+	+	+	+	
		Mild		+	+		+	+		+	+			+				+		+	+
		Severe	+			+			+			+	+		+	+	+		+		
		Acute			+		+		+	+	+				+			+		+	
		Chronic	+	+		+		+				+	+	+		+	+		+		+

Table /(contd.)

	Microbiological findings	Occ. colonies of Staph.	Staph. aureus	Staph. aureus	Staph. aureus	Coagulase positive Staph.	Staph. aureus	Staph.aureus negative
Weight	Overweight or weight gain				+		+	+ + +
Other Clinical Signs	Thermophilia				+			
	Sleepiness							
	Lethargy easily tired	+		+			+	
	Polydipsia	+						
	Polyphagia							
	Anorexia	+					+	
	False pregnancy	+						
	Lymph nodes enlarged				+			
	Anal sacs impacted							
Skin and Coat	Acanthosis	+			+			+
	Hyper-pigmentation	+ + +	+	+	+	+	+	+
	Hyperkeratosis							
	Erythema	+	+		+ + +		+	+
	Seborrhoea				+		+	
	Scaliness		+		+		+ +	+
	Thin Skin							
	Thick Skin							
	Excess Moult	+	+		+		+	
	Easily epilated			+			+	
	Alopecia				+ + + +	+	+	
Dermatitis	Pruritus		+	+ + + +	+ + + +	+	+ + + + + +	+ +
	Interdigital				+			
	Otitis	+ +	+		+		+	
	Localised	+	+	+ +	+ + +	+ + + + + + +	+	
	Generalised	+ +		+	+ +		+ + + + + + +	+ + +
	Mild	+	+	+	+ + +	+ + + + + + +	+	+ +
	Severe	+ +		+	+ + +		+ + + + +	+ +
	Acute	+		+ +	+ +	+ + + + + + +	+ + +	+ +
	Chronic	+ +	+		+ + + + + +		+ + +	+
	Dog No.	P61 P62	P63 P64	P65 P66	P67 P68 P69	P70 P71 P72 P73 P74	P75 P76 P77 P78 P79	P80 P81 P82 P83 P84 P85

Table 32 (contd.)

		Microbiological findings	P86	P87	P88	P89	P90	P91	P92	P93	P94	P95	P96	P97	P98	P99
							negative			Staph. epidermidis	Staph. aureus & diptheroids		Staph. aureus, beta-haem Group G Strep.		Diptheroids, alpha-haem Strep. Staph. aureus, staph. epidermidis	negative
		Dog No.														
Weight		Overweight or weight gain	+													
Other Clinical Signs		Thermophilia														
		Sleepiness														
		Lethargy easily tired													+	
		Polydipsia													+	
		Polyphagia														
		Anorexia														
		False pregnancy									+					
		Lymph nodes enlarged														
		Anal sacs impacted														
Skin and Coat		Acanthosis														
		Hyper-pigmentation		+							+		+			
		Hyperkeratosis														
		Erythema									+		+			
		Seborrhoea														
		Scaliness									+					
		Thin skin														
		Thick skin														
		Excess moult		+	+											
		Easily epilated														
		Alopecia		+			+									
Dermatitis		Pruritus		+		+	+					+	+		+	
		Interdigital												+		
		Otitis		+							+			+	+	
		Localised	+		+	+	+					+				
		Generalised		+				+	+	+	+		+	+	+	+
		Mild	+		+	+	+			+		+				+
		Severe		+				+	+		+		+	+	+	
		Acute	+	+	+	+									+	+
		Chronic					+	+	+	+	+	+	+	+		

Table 32 contd.

In addition to the signs listed for each dog in the main part of the Table, some dogs had other clinical signs as indicated:

Dog No.	Additional Clinical signs
P40	pendulous prepuce
P54	weight loss, dental calculus, bilateral cataract
P61	irregular oestrus, gynecomastia, enlarged vulva
P62	constipation
P85	lichenified skin

TABLE 33 Group P, Summary of Clinical Signs in Dogs with Pyoderma

Clinical Sign	No. of Dogs	Clinical Sign	No. of Dogs
Chronic inflammation	58	Thick Skin	8
Localised inflammation	56	Acanthosis	6
Pruritus	55	Hair easily epilated	6
Mild inflammation	60	Polydipsia	5
Acute inflammation	41	Sleepiness	4
Generalised inflammation	43	Hyperkeratosis	3
Severe inflammation	39	Lymph nodes enlarged	3
Hyperpigmentation	28	Seborrhoea	3
Excess moult	26	False Pregnancy	3
Otitis Externa	24	Thermophilia	3
Erythema	23	Anorexia	2
Interdigital inflamation	13	Polyphagia	2
Scaliness	12	Anal Sacs Impacted	1
Alopecia	11	Thin Skin	1
Lethargy	9		

Table 34

Group A, Clinical findings in dogs affected with allergic skin conditions

		A1	A2	A3	A4	A5	A6	A7	A8	A9	A10	A11	A12	A13	A14	A15	A16	A17	A18	A19	A20	A21	A22	A23	A24	A25	A26	A27	A28
Weight	Weight loss	+																											
	Overweight or weight gain																												
Behaviour	Thermophilia																												
	Sleepiness																												
	Pot belly																								+				
	Polyuria																												
	Polydipsia		+																				+						
	Polyphagia																												
	Anorexia	+	+																										
	Gynecomastia																												
	False pregnancy																						+						
Other Clinical Signs	Lymph nodes enlarged	+																							+			+	
	Impacted anal sacs									+		+							+										
	Acanthosis				+																								
	Hyperpigmentation				+												+							+	+	+		+	
	Hyperkeratosis																												
	Lichenified																								+				
	Lethargy																												
	Erythema	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+
	Seborrhoea																												
	Scaliness	+	+	+										+															
	Biting and pulling hair							+		+	+	+			+	+	+	+			+			+	+		+	+	
	Thin skin																												
	Thick skin				+																			+	+				
	Excess moult	+		+	+					+																			
	Easily epilated																												
	Alopecia														+										+				
Description of Dermatitis	Pruritus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	Interdigital		+																									+	
	Conjuctivitis																												
	Otitis	+													+							+							
	Localised	+		+	+	+	+	+		+		+	+		+	+		+	+	+	+	+	+	+	+	+	+		+
	Generalised		+						+		+			+			+											+	
	Mild	+	+	+	+	+	+	+			+	+	+		+	+	+		+	+	+				+		+		
	Severe							+	+	+				+				+				+	+	+		+		+	+
	Acute						+						+				+								+		+		+
	Chronic	+	+	+	+	+		+	+	+	+	+		+	+	+		+	+	+	+	+	+	+		+		+	
	Dog No.	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10	A11	A12	A13	A14	A15	A16	A17	A18	A19	A20	A21	A22	A23	A24	A25	A26	A27	A28

Table 34 contd.

		A29	A30	A31	A32	A33	A34	A35	A36	A37	A38	A39	A40	A41	A42	A43	A44	A45	A46	A47	A48	A49	A50	A51	A52	A53	A54	A55	A56	A57
Weight	Weight loss																													
	Overweight or weight gain																					+								
Behaviour	Thermophilia																													
	Sleepiness																													
	Pot belly																													
	Polyuria																													
	Polydipsia																+					+								
	Polyphagia																					+								
	Anorexia																													
	Gynecomastia								+																					
	False pregnancy																													
Other Clinical Signs	Lymph nodes enlarged												+																	
	Impacted anal sacs															+														
	Acanthosis																				+									
	Hyperpigmentation	+	+				+		+						+					+	+									
	Hyperkeratosis						+																							
	Lichenified	+													+					+										
	Lethargy			+																										
	Erythema	+	+	+	+	+	+		+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+
	Seborrhoea																							+						
	Scaliness							+	+						+	+				+										
	Biting and pulling hair			+	+						+	+	+		+			+	+		+	+			+	+			+	
	Thin skin																													
	Thick skin	+	+																	+										
	Excess moult							+								+							+							
	Easily epilated																													
	Alopecia			+	+			+		+		+												+		+			+	
Description of dermatitis	Pruritus	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	Interdigital																						+		+					
	Conjunctivitis														+							+								
	Otitis														+															
	Localised	+		+	+	+			+		+					+		+			+	+	+	+	+	+	+	+	+	
	Generalised		+				+	+		+		+	+	+	+		+		+	+										+
	Mild	+	+		+	+	+				+	+			+		+						+	+		+				
	Severe			+				+	+	+			+	+		+		+	+	+	+	+			+	+		+	+	+
	Acute	+		+			+	+			+	+	+	+		+					+		+	+		+		+	+	
	Chronic		+		+	+			+	+					+		+	+	+	+		+			+		+	+		
	Dog No.	A29	A30	A31	A32	A33	A34	A35	A36	A37	A38	A39	A40	A41	A42	A43	A44	A45	A46	A47	A48	A49	A50	A51	A52	A53	A54	A55	A56	A57

TABLE 35 Group A, Summary of Clinical Signs in Dogs with Allergic Skin Conditions

Clinical Sign	No. of Dogs	Per-centage	Clinical Sign	No. of Dogs	Per-centage
Erythema	56	98.20	Interdigital Inflammation	4	7.00
Pruritus	56	98.20	Lichenified	4	7.00
Localised Inflammation	39	68.40	Lymph Nodes Enlarged	4	7.00
Chronic Inflammation	36	63.20	Otitis Externa	4	7.00
Mild "	29	51.90	Polydipsia	4	7.00
Severe "	28	49.10	Acanthosis	2	3.50
Biting and pulling hair	26	45.60	Anorexia	2	3.50
Acute Inflammation	21	36.80	Conjunctivitis	1	1.80
Generalised Inflammation	18	31.60	False Pregnancy	1	1.80
Hyperpigmentation	13	22.80	Gynecomastia	1	1.80
Alopecia	11	19.30	Hyperkeratosis	1	1.80
Scaliness	9	15.80	Lethargy	1	1.80
Excess Moult	7	12.30	Polyphagia	1	1.80
Thick Skin	6	10.50	Pot Belly	1	1.80
Anal Sac Impacted	4	7.00	Seborrhoea	1	1.80
			Lethargy	1	1.80

Table 36

Group EP, Clinical findings in dogs with external parasitism

		EP1	EP2	EP3	EP4	EP5	EP6	EP7	EP8	EP9	EP10	EP11	EP12	EP13	EP14	EP15	EP16	EP17	EP18	EP19	EP20	EP21	EP22	EP23	EP24	EP25	EP26	EP27	EP28	EP29
Weight	Weight loss																													
	Overweight or weight gain																													+
Behaviour	Thermophilia																													
	Sleepiness																													
	Pot belly																													
	Polyuria																													+
	Polydipsia																													
	Polyphagia																													+
	Anorexia										+																			
	False pregnancy																													
Other Clinical Signs	Lymph nodes enlarged				+																									+
	Impacted anal sacs										+																			
	Acanthosis															+														
	Hyper-pigmentation		+	+												+							+							
	Hyperkeratosis																													
	Lichenified																				+									
	Lethargy																													
	Erythema	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
	Seborrhoea																					+								
	Scaliness	+		+		+						+						+					+		+					
	Pulling hair	+				+					+			+	+	+					+	+		+	+	+		+	+	
	Thin skin																													
	Thick skin			+						+	+					+	+			+			+	+						
	Excess moult																													
	Easily epilated						+																							
	Alopecia		+	+		+	+				+		+												+	+	+		+	+
Description of Dermatitis	Pruritus	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	
	Interdigital				+																							+		
	Otitis			+																	+									
	Localised					+	+			+	+			+	+	+	+	+			+			+						
	Generalised	+	+	+	+			+	+			+	+						+	+		+	+		+	+	+	+	+	+
	Mild					+					+													+						
	Severe	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+
	Acute					+		+	+	+	+	+		+	+	+	+			+	+			+	+	+		+		+
	Chronic	+	+	+	+		+						+					+	+			+	+				+		+	
	Dog No.	EP1	EP2	EP3	EP4	EP5	EP6	EP7	EP8	EP9	EP10	EP11	EP12	EP13	EP14	EP15	EP16	EP17	EP18	EP19	EP20	EP21	EP22	EP23	EP24	EP25	EP26	EP27	EP28	EP29

Table 36 (contd.)

		EP30	EP31	EP32	EP33	EP34	EP35	EP36	EP37	EP38	EP39	EP40	EP41	EP42	EP43	EP44	EP45	EP46	EP47	EP48	EP49
Weight	Weight loss																				
	Overweight or weight gain																				
Behaviour	Thermophilia																				
	Sleepiness																				
	Pot belly																				
	Polyuria																				
	Polydipsia																				
	Anorexia																				
	False pregnancy																				
Other Clinical Signs	Lymph nodes enlarged					+	+														
	Impacted anal sac		+					+													
	Acanthosis																				
	Hyperpigmentation								+												
	Hyperkeratosis																				
	Lichenified																				
	Lethargy																				
	Erythema	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+		+
	Seborrhoea																				
	Scaliness																				+
	Pulling hair	+	+		+	+	+	+	+	+			+	+	+			+	+		
	Thin skin																				
	Thick skin															+					
	Excess moult																		+		
	Easily epilated																				
	Alopecia	+	+				+				+				+						
Description of Dermatitis	Pruritus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+
	Interdigital																				
	Otitis																				
	Localised		+	+	+	+		+				+	+	+						+	
	Generalised	+					+		+	+	+				+	+	+	+	+		+
	Mild		+	+	+	+			+		+	+	+					+			
	Severe	+						+		+				+	+	+	+		+	+	+
	Acute	+	+		+	+	+	+	+	+	+		+	+	+			+	+	+	
	Chronic			+								+				+	+				+
	Dog No.	EP30	EP31	EP32	EP33	EP34	EP35	EP36	EP37	EP38	EP39	EP40	EP41	EP42	EP43	EP44	EP45	EP46	EP47	EP48	EP49

TABLE 37 Group EP, Summary of Clinical Signs in Dogs with External Parasites

Clinical Sign	No. of Dogs	Percentage
Erythema	46	93.90
Pruritus	46	93.90
Severe inflammation	37	75.50
Acute inflammation	32	65.30
Generalised inflammation	29	59.20
Pulling hair	26	53.10
Localised inflammation	20	40.80
Chronic inflammation	17	34.70
Alopecia	16	32.70
Mild inflammation	12	24.50
Thick skin	9	18.40
Scaliness	8	16.30
Hyperpigmentation	5	10.20
Anal sac impacted	3	6.10
Lymph Node enlarged	3	6.10
Acanthosis	1	2.00
Anorexia	1	2.00
Easily epilated hair	1	2.00
Excess moult	1	2.00
Interdigital inflammation	1	2.00
Lichenified	1	2.00
Otitis Externa	1	2.00
Pale Mucosa	1	2.00
Seborrhoea	1	2.00

BODY WEIGHT

Most of the dogs were weighed on first presentation and subsequently. The weights given for breeds by Hubbard (1964) were taken as standards, and judgements were made as to whether a dog was under or overweight or of normal weight for its stage of growth, at the time of first examination. The number of dogs weighed in each group, the number considered to be overweight and the statistical analysis of these data are shown in Tables 38 and 39 .

The statistical analysis indicates that there is no significant difference between the OH, P, A and EP groups but they are significantly different from the N and HS groups. The normal and hypothyroidism suspected group are significantly different from each other ($P < 0.001$), with 13.9% and 78.7% overweight respectively.

Table 38

Number of overweight dogs in each group

Group	No. of dogs weighed	No. overweight	Percentage
N	36	5	13.9
HS	43	37	78.7
OH	34	16	47.1
P	63	27	42.9
A	36	14	38.9
EP	24	7	29.2

	Degree of freedom	Chi-square	
All	5	44.427	***
All less N	4	27.796	***
All less HS	4	11.386	**
All less N & HS	3	2.607	

P*** < 0.001 P** < 0.05

Table 39

Number of overweight dogs in the normal (N) and hypothyroidism suspected (HS) groups

Group	No. of dogs weighed	No. overweight	Chi-square
N	36	5	
HS	43	37	12.412

P *** < 0.001

INCIDENCE

Breeds of Dogs with Suspected Hypothyroidism

Results

The 47 cases of suspected hypothyroidism involved 22 breeds or breed types (see Table 40).

Table 40

Numbers of dogs, by breeds, with suspected hypothyroidism

Large breeds	No.	Medium sized breeds	No.	Small breeds	No.
Airedale	3	Beagle	1	Cairn	4
Boxer	1	Tibetan T.	1	Corgi	1
Collie X	1			Dachshund	3
Chow	1			Lakeland T.	1
Doberman	3			Poodle	3
I. setter	3			Poodle X	1
Labrador	8			Scot. T.	2
P M D	1			S H F T	1
Spaniel	1			Shetland C.	1
				W H W	4
				Yorkie	2
Total	22		2		23

Age of Dogs with Suspected Hypothyroidism

Results

The age distribution of the HS cases is given in Table 41.

The age ranged from 10 weeks to 13 years, with cases occurring at all ages from 2 years.

Sex of Dogs with Suspected Hypothyroidism

Results

The distribution of male, castrated male, female and neutered female dogs in the 47 suspected hypothyroidism cases was 14, 1, 29 and 3 respectively or 29.79, 2.13, 61.70 and 6.38 per cent respectively.

Table 41 Age of suspected hypothyroid dog, when presented

Age:	< 6m	6-11m	1y	2y	3y	4y	5y	6y	7y	8y	9y	10y	11y	12y	13y	Total
Male	1			1	1	1		1	1		1	4		2	1	14
Male n.					1											1
Female	1			3	4	1	1	1	6	3	3	1	2	2	1	29
Female n.						1					1			1		3
Total	2			4	6	3	1	2	7	3	5	5	2	5	2	47

SKIN THICKNESS

Results

The measurement of skin thickness, obtained from the 15 sites on each dog, are recorded in Tables 42, 43, 44, 45 for Groups 1, 2, 3 and 4 respectively. Tables 46 and 2 give the abbreviations used for skin sites and breed of dog, respectively. For each group, the mean and standard deviation of the measurements at each site are given in Table 47. The mean and standard deviation of the measurements at each site, for each breed, irrespective of the dog's state of health are given in Table 48.

One-way analyses of variance was performed on the data (Table 47). There was only one skin site with a statistically significant difference in thickness, in the 4 groups of dogs. This was the groin and none of the other sites showed any significant difference between the groups. In order to detect where the significance lay between the 4 groups of dogs in respect of the groin, the data were examined by Duncan's multiple range test to obtain significant subsets. The results of this are shown in Table 49 the skin thickness of the groin in Group 2 (hypothyroid dogs) differed significantly from that of the dogs in Group 1 (normal) and Group 4 (dogs with non-hormonal conditions) but did not differ significantly from that of the dogs with other hormonal conditions, Group 3. The thickness of groin skin did not differ significantly between Groups 1, 3 and 4. The f, or variance, ratio of the groin skin thickness was 2.95 and the degree of significance $P < 0.05 > 0.01$.

Having ascertained this difference between the groups, the data were re-worked by the same methods to investigate whether there were significant differences in skin

thickness between the sites in each group. Table 50 shows the subsets obtained by Duncan's multiple range test. In each group of dogs, there were significant differences between sites. None of the three abnormal groups (2, 3 and 4) had a single site that was significantly different from all of the other 14 sites. The smallest homogeneous subset in these three groups of dogs contained two sites. In the normal dogs (Group 2), the nose and lumbo-sacral region each formed their own subset.

The data from the dogs were re-assembled (see Table 48) to provide a list of mean and standard deviations of the measurements, by the breed of dog, irrespective of whether the animals were normal or otherwise. This was subjected to the same statistical analyses as above and it was ascertained by one-way analyses of variance and Duncan's multiple range test that there were statistically significant differences between the breeds in respect of the following sites, chest, throat, ear margin, ear pinna, lumbo-sacral region, hip, withers, and lumbar region. The degree of significant difference varied from $P < 0.01$ to $< 0.05 > 0.01$. The 7 other sites, including the groin, did not show this difference. For the 8 sites in which breed differences were statistically significant Table 51 was prepared to ascertain the significant subsets by Duncan's multiple range test, and it shows the complex nature of the relationships. Between groups of breeds, the number of homogeneous subsets varied from two to five, i.e. there was no single site in a single breed which was significantly different from all others.

TABLE 42 Skinfold thickness (mm) in group 1, normal dogs.

Dog No.	Age (years)	Sex	Breed	Wt. (kg)	AX	GR	AB	CH	TR	LP	NO	KM	KP	LG	LS	HP	WI	LU	KL
122269	-	M	Box	-	2	3	3	4	5	5	8	2	3	3	6	4	6	6	5
Kelly	-	F	Box	-	2	2	3	4	4	3	6	3	2	3	6	6	5	5	3
118541	10	M	Spa	15	3	3	5	5	6	3	6	3	4	5	8	7	8	6	4
110581	2 10/12	M	Spa	10.7	2	2	4	4	3	2	6	3	3	4	7	6	5	5	3
123950	4	F	I.Set	-	2	2	3	3	3	3	4	2	2	3	6	6	6	5	3
120700	2 6/12	M	Box.X Als	29.7	2	2	3	4	4	3	6	2	3	3	8	6	7	5	3
120614	2 6/12	M	Grey	35	1	1	1	1	2	2	2	2	2	1	2	2	2	2	2
120329	1 6/12	F	Ter	20	2	2	3	4	3	2	5	2	2	3	8	7	8	6	3
120616	4 6/12	M	Ter	24.3	2	2	3	6	4	2	6	2	2	4	8	6	10	6	3
120625	2	M	Ter	15.3	2	2	5	6	4	3	6	2	2	4	10	10	9	7	2
120697	6 6/12	M	WHFT	13.8	3	2	5	5	5	4	7	2	3	7	16	13	14	11	4
120563	5	F	Ter	-	2	2	3	3	3	2	3	2	2	3	5	5	6	4	2
121084	5	M	Ter	-	2	1	2	4	3	1	4	1	2	3	8	4	8	5	2
3462(A)	11	F	Lab	21	3	3	6	8	7	3	5	4	3	5	9	8	10	6	4
115016	1 7/12	M	Lab	29.3	2	3	4	5	6	3	8	3	2	6	12	7	9	9	4
115638	11	M	Lab	-	4	2	5	6	4	3	4	3	3	4	6	7	8	6	3
116456	4/12	F	Lab	25	2	3	7	5	4	2	6	2	3	6	11	7	8	8	3
114823	3 6/12	F	Cai	9.6	2	2	4	6	6	3	6	2	3	4	20	12	14	12	4
109335	3	M	Cai	8	2	2	4	6	4	3	4	1	2	4	9	8	10	7	3
101247	5 5/12	M	WHW	7.7	2	2	4	4	4	2	5	1	2	2	7	6	6	7	2
121031	10/12	F	Col.X	12.7	2	1	2	3	2	2	4	1	1.5	2	5	4	4	4	2
121384	2 6/12	F	R.Col	16.5	3	2	8	7	2	2	3	1	2	3	7	8	7	8	3
120796	1	M	B.Col	13.2	2	2	2	2	2	2	4	1	2	3	4	3	3	4	3
120384	8/12	F	Col.X	20	2	1	4	3	4	2	3	1	1	3	10	8	6	7	2
Ann(151)	5	F	Col.X	10	5	2	4	5	4	4	7	3	2	4	9	6	11	7	5
106455	14	F	Col.X	9	4	3	5	6	5	3	6	3	2	4	8	6	7	8	3
113057	2	M	Col.X	17	2	2	2	3	4	2	3	1	2	3	6	4	4	5	4
120352	6	M	Poo	14	5	1	4	4	5	2	3	3	3	5	4	3	3	3	4
106839	5	M	Als	-	2	2	3	4	4	2	6	2	2	4	9	9	8	8	3
120789	6/12	M	PMD	42	3	3	4	5	4	3	5	2	3	4	13	9	6	10	4
120908	4/12	M	Poi	-	2	2	2	3	3	3	4	1	2	3	6	3	5	5	3
121120	8/12	M	Ter	-	2	2	3	3	3	2	3	2	2	3	5	5	6	4	2
111807	5/12	F	Ret	30	3	2	4	8	4	2	5	2	3	6	10	10	9	11	2
122270	3	M	Ter	-	2	1	2	3	4	2	4	2	2	4	6	4	4	4	3
120725	8	F	Ter	9.5	2	2	3	2	2	2	3	1	2	2	5	4	5	4	2
				Mean	2.43	2.03	3.68	4.4	3.88	2.54	4.85	2.0	2.33	3.71	7.97	6.37	7.06	6.28	3.06
				SD	0.88	0.62	1.47	1.63	1.23	0.78	1.54	0.80	0.60	1.27	3.47	2.54	2.8	2.33	0.87

TABLE 43 Skinfold thickness (mm) in group 2, hypothyroid dogs.

Dog No.	Age (years)	Sex	Breed	Wt. (kg)	AX	GR	AB	CH	TR	LP	NO	EM	EP	LG	LS	HP	WI	LU	EL
17 HS	7	F	Lab	34	3	3	3	7	6	3	6	3	3	4	12	7	12	7	3
5 HS	2	F	Lab	36.5	2	2	4	5	5	3	6	3	3	6	17	10	14	10	3
14 HS	3	F	Sco	11	3	3	4	6	5	3	5	2	2	4	18	8	12	12	3
13 HS	10	M	Air	34	5	3	5	5	4	2	5	2	2	3	5	6	8	6	4
4 HS	2	F	Dac	11.5	2	2	2	3	3	2	5	2	2	3	6	3	4	4	3
2 HS	13	M	Poc	12.4	4	2	3	5	4	2	4	3	2	4	4	5	7	6	3
33 HS	10 6/12	F	WHW	8	3	3	4	4	5	2	6	1	2	5	9	6	10	8	2
21 HS	6	M	WHW	13	3	3	4	7	3	3	5	1	2	6	8	6	8	3	3
11 HS	8	F	WHW	9.5	3	6	6	10	7	3	5	1	3	4	7	6	12	8	4
12 HS	13	F	Cai	5.9	3	2	4	4	4	2	4	1	2	3	12	10	10	12	2
24 HS	10 wks	F	PMD	42	2	2	7	5	4	3	4	1	2	4	10	9	8	8	2
26 HS	7	F	SHPT	9.2	1	1	3	3	3	2	3	2	5	5	8	4	2	5	2
				Mean	2.83	2.66	4.08	5.38	4.42	2.50	4.83	1.83	2.50	4.25	9.66	6.66	8.91	7.41	2.83
				SD	1.03	1.23	1.38	1.97	1.24	0.52	0.94	0.83	0.90	1.05	4.42	2.22	3.50	2.87	0.71

TABLE 44 Skinfold thickness (mm) in group 3, dogs with 'other hormonal' conditions

Dog No.	Age (years)	Sex	Breed	Wt. (kg)	Condition	AX	GR	AB	CH	TR	LP	NO	EM	EP	LG	LS	HP	WI	LU	EL
9 OH	13	F	Pek	7	Cush.synd.	3	2	3	2	3	3	4	2	2	4	6	4	5	5	3
11 OH	8	M	G.Ret	30	iatrogenic Cushing's	4	3	4	10	6	2	4	3	3	5	10	6	12	12	4
37 OH	5 5/12	F	Sco	19	overweight	3	4	5	6	4	2	7	1	2	16	15	10	15	11	6
25 OH	8	M	Ter	18.5	Cush.synd.	1	1	1	2	2	2	3	2	2	2	3	2	4	2	3
119817	2 2/12	M	B.Ter	6	diabetic	4	3	4	6	6	2	4	2	3	4	12	7	15	12	4
120598	9 6/12	FN	Sco	9.5	cirrhosis of liver	2	2	4	4	4	2	3	1	2	2	12	7	8	6	2
108230	8 9/12	M	Spa	26.6	diabetic	3	3	6	5	4	3	7	2	4	3	7	8	12	8	3

	AX	GR	AB	CH	TR	LP	NO	EM	EP	LG	LS	HP	WI	LU	EL
Mean	2.86	2.57	3.86	5.00	4.14	2.29	4.57	1.86	2.57	5.14	9.29	6.29	10.12	8.00	3.57
SD	1.07	0.98	1.57	2.79	1.46	0.49	1.72	0.70	0.79	4.91	4.15	2.62	4.52	3.87	1.27

TABLE 45 Skinfold thickness (mm) in group 4, dogs with non-hormonal skin conditions.

Dog No.	Age (years)	Sex	Breed	Wt. (kg)	Condition	AX	GR	AB	CH	TR	LP	NO	EM	EP	LG	LS	HP	WI	LU	EL
6D	1	M	Lab	20.5	demodectic m.	3	2	3	7	4	2	4	1	2	4	8	6	9	7	6
122720	2 9/12	M	Lab	-	pyoderma	4	3	6	8	5	3	6	4	7	5	7	14	11	10	8
26A	3	F	Lab	-	contact dermatitis	3	2	4	5	5	3	6	3	3	4	8	4	8	6	4
27EP	1	M	Ter	20	demodectic m.	2	1	4	4	4	3	4	2	2	4	9	4	6	5	2
77P	6/12	M	Ter	15.5	dermatitis	2	2	2	3	2	3	3	2	2	4	8	4	6	5	2
25A	6	MN	B.Ter	11.5	contact dermatitis	2	2	3	4	7	4	6	2	2	5	10	6	15	7	4
18P	5 6/12	M	Box	33.8	pyoderma	2	3	4	5	6	4	6	3	3	5	10	6	11	7	5
49EP	2 6/12	F	Sco	7.8	demodectic m.	2	2	1	5	4	2	3	3	3	6	12	14	8	7	3
28EP	6	F	Spa	15.3	demodectic m.	4	3	5	8	8	7	6	4	3	9	9	3	10	6	1
30EP	1	M	Spa	13.5	demodectic m.	2	2	3	3	5	2	4	2	2	3	5	3	5	6	3
19BP	3	M	OES	26.8	dermatitis	3	2	6	6	3	3	7	2	3	5	12	10	16	11	4
34A	5	F	Beard Col	-	pruritus and alopecia	2	2	2	4	3	3	4	2	2	3	5	4	7	5	3
42A	5/12	M	Bea	-	allergic d.	2	1	2	4	4	2	4	1	2	3	6	4	4	6	2
17P	6/12	M	Lur	24.8	dermatitis	1	1	2	2	3	2	5	1	2	3	3	3	3	3	2
120418	3	M	Als	32	demodectic m.	3	3	5	5	5	3	5	2	2	5	10	6	8	7	3
EP	3/12	M	Poo	-	sarcoptic m.	2	1	2	2	3	2	3	4	2	3	4	3	3	3	2
39P	8	M	Col	30	epidermitis	2	2	6	5	4	2	7	2	4	4	11	10	14	14	3
100131	5/12	F	Col.X	29.5	demodectic m.	3	3	5	3	3	2	4	2	2	4	6	4	3	5	3
120615	6 6/12	M	Col.X	16	dermatitis	2	2	3	4	4	2	5	2	3	4	7	5	6	4	4
48P	8	M	WHW	8.7	epidermitis	3	3	3	4	4	2	5	2	2	3	15	10	8	10	2
24P	11	FN	WHW	-	epidermitis	3	2	4	6	4	2	2	3	3	4	8	6	10	6	3
3EP	-	F	Cai	10.8	demodectic m.	3	2	4	6	4	2	5	2	2	5	10	11	11	8	4
10219	12	F	Cai	4	dermatitis	2	2	2	4	5	3	5	2	2	3	10	8	10	6	3
24A	-	M	Cai	7	fl. allergic dermatitis	2	2	2	3	4	3	5	2	2	3	14	5	7	10	3
7EP	2 9/12	F	CKC	3	-	2	1	2	3	3	3	3	2	2	3	4	3	4	4	2
14EP	5 6/12	F	CKC	4.5	sarcoptic m.	3	2	3	3	2	2	5	3	3	4	7	3	6	6	3
18A	3/12	F	G.Ret	25	dermatitis	3	2	5	5	5	3	5	2	3	4	8	6	8	7	3
P	1 3/12	M	G.Da	-	labial d.	2	2	3	3	3	3	5	3	2	4	7	5	8	6	4
108967	12	M	Lab	30	dermatitis	3	2	5	8	6	3	5	2	4	3	10	8	14	10	4
103545	3 7/12	F	Lab	28.5	epidermitis	3	3	4	5	4	2	4	1	2	2	14	9	11	8	3
					Mean	2.5	2.06	3.5	4.56	4.2	2.73	4.7	2.26	2.6	4.03	8.56	5.9	8.33	6.83	3.27
					SD	0.68	0.64	1.41	1.67	1.35	1.01	1.20	0.83	1.03	1.3	3.02	2.87	3.54	2.46	1.36

TABLE 46

Abbreviations used in Tables and Figures referring to skin thickness measurements

Skin site	Abbreviation
Lip	LP
Nose	NO
Eyelid	EL
Ear margin	EM
Ear pinna	EP
Throat	TR
Chest	CH
Axilla	AX
Abdomen	AB
Groin	GR
Lower part of leg	LG
Hip	HP
Withers	WI
Lumbar region	LU
Lumbo-sacral region	LS

TABLE 47 Skinfold thickness (mean and standard deviation (SD)), (mm) at 15 sites in dogs of groups 1 to 4.

Group	Number		Axilla	Groin	Abdomen	Chest	Throat	Lip	Nose
1	35	Mean	2.43	2.03	3.68	4.40	3.88	2.54	4.85
		SD	0.88	0.62	1.47	1.63	1.23	0.78	1.54
2	12	Mean	2.83	2.66	4.08	5.33	4.42	2.50	4.83
		SD	1.03	1.23	1.38	1.97	1.24	0.52	0.94
3	7	Mean	2.90	2.60	3.80	5.00	4.14	2.28	4.57
		SD	1.07	0.97	1.57	2.77	1.46	0.40	1.72
4	30	Mean	2.50	2.06	3.50	4.56	4.20	2.73	4.70
		SD	0.68	0.64	1.41	1.67	1.35	1.01	1.20
		Variance ratio	1.09	2.95*	0.48	0.91	0.64	0.71	0.12

*P = <0.05 >0.01

Group	Number		Ear Margin	Ear Pinna	Leg	Lumbo-Sacral	Hip	Withers	Lumbar	Eye Lid
1	35	Mean	2.00	2.33	3.71	7.97	6.37	7.06	6.28	3.06
		SD	0.80	0.60	1.27	3.47	2.54	2.80	2.33	0.87
2	12	Mean	1.83	2.50	4.24	9.66	6.66	8.91	7.41	2.83
		SD	0.83	0.90	1.05	4.42	2.22	3.50	2.87	0.71
3	7	Mean	1.85	2.57	5.14	9.28	6.28	10.14	8.00	3.57
		SD	0.70	0.78	4.91	4.15	4.15	4.52	3.87	1.27
4	30	Mean	2.26	2.60	4.03	8.56	5.90	8.33	6.83	3.27
		SD	0.83	1.03	1.30	3.02	2.87	3.54	2.46	1.36
		Variance ratio	1.16	0.61	1.31	0.81	0.27	2.29	1.18	0.90

Group 1 : Normal Dogs
Group 2 : Hypothyroid suspected cases.
Group 3 : "Other hormonal" skin diseases
Group 4 : Non-hormonal skin diseases

TABLE 48 Skinfold thickness in different breeds.

Breed	No. of dogs		AX	OR	AB	CH	TR	LP	MO	EM	EP	LO	LS	HP	WI	LU	EL
Ter	13	Mean	2.08	1.84	2.92	3.85	3.61	2.30	4.15	1.85	2.00	3.46	7.46	5.23	7.85	5.46	2.61
		SD	0.64	0.55	1.03	1.41	1.50	0.75	1.21	0.38	0.00	0.87	2.55	2.01	3.65	2.40	0.76
WHW	6		2.83	3.17	4.17	5.83	4.50	2.33	4.67	1.50	2.33	4.00	9.00	6.67	9.00	7.00	2.67
			0.41	1.47	0.98	2.40	1.38	0.52	1.37	0.84	0.52	1.41	3.03	1.63	2.10	2.37	0.82
Col.X	7		2.86	2.00	3.57	3.86	3.71	2.42	4.57	1.86	1.93	3.43	7.29	5.29	5.86	5.71	3.29
			1.21	0.82	1.27	1.21	0.95	0.79	1.51	0.90	0.61	0.79	1.80	1.50	2.67	1.60	1.11
Col	4		2.25	2.00	4.50	4.50	2.75	2.25	4.50	1.50	2.50	3.25	6.75	6.25	7.75	7.75	3.00
			0.50	0.00	3.00	2.08	0.96	0.50	1.73	0.58	1.00	0.50	3.10	3.30	4.57	4.50	0.00
Lab	11		2.91	2.55	4.65	6.27	5.10	2.73	5.45	2.63	3.18	4.45	10.36	7.91	10.36	7.91	4.10
			0.70	0.52	1.29	1.35	1.04	0.48	1.21	1.03	1.40	1.29	3.26	2.55	2.25	1.64	1.58
Cai	6		2.33	2.00	3.33	4.83	4.50	2.66	4.83	1.67	2.17	3.66	12.50	9.00	10.33	9.16	3.17
			0.52	0.00	1.03	1.33	0.84	0.52	0.75	0.52	0.41	0.82	4.09	2.53	2.25	2.56	0.75
Spa	5		2.80	2.60	4.60	5.00	5.20	3.40	5.80	2.80	3.20	4.80	7.20	5.40	8.00	6.20	2.80
			0.84	0.55	1.14	1.87	1.92	2.07	1.10	0.84	0.84	2.49	1.48	2.30	3.08	1.10	1.10
Soo	4		2.50	2.75	3.50	5.25	4.25	2.25	4.50	1.75	2.25	7.00	14.25	7.25	10.75	9.00	3.50
			0.57	0.96	1.73	0.96	0.50	0.50	1.91	0.95	0.50	6.22	2.87	2.50	3.40	2.94	1.73
Box	3		2.00	2.66	3.33	4.33	5.00	4.00	6.66	2.66	2.66	3.66	7.33	5.33	7.33	6.00	4.33
			0.00	0.58	0.58	0.57	1.00	1.00	1.15	0.58	0.58	1.15	2.31	1.15	3.21	1.00	1.15
Ret	3		3.33	2.33	4.33	7.66	5.00	2.33	4.66	2.33	3.00	5.00	9.33	7.33	9.66	10.00	3.00
			0.57	0.57	0.57	2.52	1.00	0.57	0.57	0.57	0.00	1.00	1.15	2.31	2.08	2.65	1.00
Poo	3		3.66	1.33	3.00	3.66	4.00	2.00	4.00	2.67	2.33	4.00	3.66	3.66	4.33	4.00	3.00
			1.53	0.58	1.00	1.53	1.00	0.00	1.00	0.58	0.58	1.00	0.57	1.15	2.31	1.73	1.00
KCS	2		2.50	1.50	2.50	3.00	2.50	2.50	4.00	2.50	2.50	3.50	5.50	3.00	5.00	5.00	2.50
			0.71	0.71	0.71	0.00	0.71	0.71	1.41	0.71	0.71	0.71	2.12	0.00	1.41	1.41	0.71
PMD	2		2.50	2.50	5.50	5.00	4.00	3.00	4.50	1.50	2.50	4.00	11.50	9.00	7.00	9.00	3.00
			0.70	0.70	2.12	0.00	0.00	0.00	0.70	0.70	0.70	0.00	2.12	0.00	1.41	1.41	1.41
Als	2		2.50	2.50	4.00	4.50	4.50	2.50	5.50	2.00	2.00	4.50	9.50	7.50	8.00	7.50	3.00
			0.70	0.70	1.41	0.71	0.71	0.71	0.71	0.00	0.00	0.71	0.71	2.12	0.00	0.71	0.00
Pek	1		3	2	3	2	3	3	4	2	2	4	6	4	5	5	3
Air	1		5	3	5	5	4	2	5	2	2	3	4	6	8	6	4
I.Set	1		2	2	3	3	3	3	4	2	2	3	6	6	6	5	3
G.Dane	1		2	2	3	3	3	3	5	3	2	4	7	5	8	6	4
OES	1		3	2	6	6	3	3	7	2	3	5	12	10	16	11	4
WHPT	1		3	2	5	5	5	4	7	2	3	7	16	13	14	11	4
SHPT	1		1	1	3	3	3	2	3	2	5	5	8	4	2	5	2
Box.X Als	1		2	2	3	4	4	3	5	2	3	3	8	6	7	5	3
Poi	1		2	2	2	3	3	3	4	1	2	3	6	3	5	5	3
Ore	1		1	1	1	1	2	2	2	2	2	4	2	2	2	2	2
Dac	1		2	2	2	3	3	2	5	2	2	3	6	3	4	4	3
Bea	1		2	1	2	4	4	2	4	1	2	3	6	4	4	6	2
Lur	1		1	1	2	2	3	2	5	1	2	3	3	3	3	3	2

SITE	SUBSETS
Groin	N NH OH HS

N : Gp. 1, normal dogs
HS : Gp. 2, hypothyroid dogs
OH : Gp. 3, dogs with "other hormonal" diseases
NH : Gp. 4, dogs with non-hormonal skin conditions

TABLE 49 Groin skinfold thickness in dogs of Groups 1 to 4, significant subsets by Duncan's multiple range.

Group	Subsets, skin sites	Variance ratio
1 N	EM GR | EP AX LP | EL | AB LG TR | CH | NO | LU HP WI | LS	43.332**
2 HS	EM | EP LP | GR EL AX | AB LG | TR | NO | CH | HP | LU | WI | LS	18.198**
3 OH	EM | LP EP GR | AX EL AB | TR | NO | CH LG | HP | LU | LS | WI	6.100**
4 NH	GR EM | AX EP LP | EL AB | LG TR | CH NO | HP LU | WI LS	39.567**

** $P < 0.01$

Group 1 : normal dogs Group 2 : hypothyroid cases Group 3 : "other hormonal" disease cases Group 4 : non-hormonal skin disease cases.

TABLE 50 Skinfold thickness at 15 sites in dogs of Groups 1 to 4, significant subsets of skin by Duncan's multiple range.

SITE	VARIANCE RATIO	SUBSETS, Breed of Dog.
CH	2.72**	KCS POO TER COL X BOX ALS COL CAI PMD SPA SCO WHW LAB RET
TR	2.12*	KCS COL TER COL X PMD POO SCO ALS CAI WHW RET BOX LAB SPA
EM	2.10*	PMD COL WHW CAI SCO TER COL X ALS RET KCS LAB BOX POO SPA
EP	2.05*	COL X ALS TER CAI SCO POO WHW PMD KCS COL BOX RET LAB SPA
LS	4.40**	KCS COL SPA COL X BOX TER WHW RET ALS PMD LAB POO CAI SCO
HP	2.78**	KCS POO TER COL X BOX SPA COL WHW SCO RET ALS PMD LAB CAI
WI	2.05*	POO KCS COL X PMD BOX COL TER ALS SPA WHW RET CAI LAB SCO
LU	2.64**	KCS COL X BOX SPA WHW ALS COL LAB PMD SCO POO TER CAI RET

*P <0.05 >0.01
**P <0.01

TABLE 51 **Skinfold thickness at 8 sites, significant subsets of breeds of dog by Duncan's multiple range.**

STAGES OF HAIR CYCLE IN HYPOTHYROID AND OTHER DOGS

Results

The results of the examination of the hair are set out in Table 52 for the normal dogs which were examined at monthly intervals (Group 1). The results of groups 2 to 8 are presented in Tables 53 to 59 respectively. In some of the tables, the percentage of the hairs in the anagen phase only is given. The remainder of the hairs to complete 100 per cent were in the telogen phase.

TABLE 52

Percentage of hair in anagen phase in 10 normal dogs, examined monthly (December 1977 - November 1978)

Dog's No.	Dec.	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept	Oct.	Nov.	Mean ± S.D.
NA1	20	14	26	15	3	0	1	13	18	13	8	11	12.9 ± 7.10
NA2	17	13	0	0	0	0	3	0	0	0	31	8	14.7 ± 10.60
NA3	7	30	24	10	16	7	1	7	0	4	12	0	11.7 ± 9.10
NA4	89	87	90	85	79	81	82	85	68	94	79	87	83.70 ± 6.80
NA5	59	22	42	9	5	3	28	18	39	28	16	24	24.5 ± 16.30
NA6	2	0	0	0	0	0	0	0	0	0	0	0	1.70 ± 0.0
NA7	72	55	73	77	66	65	53	44	53	52	52	82	62.10 ± 12.00
NA8	0	16	15	0	0	0	1	0	5	0	4	0	8.10 ± 7.10
NA9	0	0	0	2	5	0	0	0	0	6	0	3	3.95 ± 1.20
NA10	0	0	0	0	0	0	0	0	0	0	0	0	-

TABLE 53

PROPORTIONS OF ANAGEN AND TELOGEN HAIR

GROUP TWO, NORMAL DOGS B (10), HAIR EXAMINED ONCE ONLY

No.	Breed	Age (years)	Sex	Date of Examination	Percentage A	Hair in T
NB1	Cairn	3.6/12	F	5.7.76	52	47
NB2	Terrier	3	F	13.7.76	46	54
NB3	Cairn	3	M	5.8.76	70	30
NB4	Collie-x	10/12	F	5.8.76	27	73
NB5	Terrier	5	F	12.8.76	0	100
NB6	Boxer-x-Alsatian			7.7.76	0	100
NB7	Labrador-x	11	F	7.7.76	0	100
NB8	Terrier			1.12.76	0	100
NB9	Boxer			1.12.76	2	98
NB10	Boxer		F	13.1.77	0	100

A : Hair in anagen phase T : Hair in telogen phase

M : Male F : Female

TABLE 54

PROPORTIONS OF ANAGEN AND TELOGEN HAIR

Group Three. Dogs with (suspected) hypothyroidism (24)

No.	Breed	Age (years)	Sex	Date of Examination	Percentage A	Hair in T
HS2	Poodle	12	M	1.11.76	100	0
HS3	*Boxer	4	Fn	6.7.78	1	99
HS5	*Labrador	2	Fn	29.6.78	0	100
HS6	Labrador	1.2/12	F	25.7.77	0	100
HS7	W.H.Dachs.	7.6/12	F	14.7.78	50	50
HS10	Poodle-x	10	Fn	10.2.77	36	64
HS11	W.H.White	8	F	2.3.77	78	22
HS12	Cairn	13	F	3.6.76	73	27
HS13	Airedale	10	M	31.3.77	65	35
HS14	Scottish T.	5	F	27.6.78	29	71
HS15	Labrador	4.6/12	M	18.7.78	0	100
HS18	Yorkshire Terrier	9	Fn	28.1.77	74	26
HS21	W.H.White	6	M	18.11.76	95	5
HS22	Yorkshire Terrier	4	M	15.12.76	88	12
HS23	Irish Setter	2	M	3.2.77	2	98
HS24	Pyrenean Mountain Dog	10wks	F	4.11.76	70	30
HS25	Cairn	12	F	23.11.76	72	28
HS26	S.H.Fox Terr.	7	F	16.2.77	2	98
HS27	Shetland collie	4	F	22.7.77	0	100
SH28	Cairn	2.6/12	F	17.2.77	84	16
HS29	Collie-x	11	F	2.3.77	2	98
HS30	Chow	4/12	M	7.3.77	19	81
HS33	W.H.White	9	F	9.11.76	97	3
HS35	Lakeland	12	F	18.3.77	88	12

A : Hair in Anagen, T : Hair in Telogen

M : Male, Mn : neutered male,
F : Female, Fn : neutered female

* Hairs were counted during the regrowth of hair after treatment, and from newly grown hair on the bald area.

TABLE 55

PROPORTION OF ANAGEN HAIR

Group Four. Dogs with conditions not affecting the hair (7)

No.	Breed	Age (Years)	Sex	Disorder	Date of Examination	Percentage of hair in Anagen
NS1	Pyrenean Mountain Dog	6/12	M	diarrhoea	13.7.76	15
NS2	Pointer	4/12	M	vomiting & diarrhoea	5.8.76	3
NS3	Hungarian vizslas	4 6/12	F	cystitis	12.8.76	0
NS4	Terrier	5	M	vert. disc	13.8.76	3
NS5	Terrier	8/12	M	road accident	13.8.76	25
NS6	Terrier	6/12	M	" "	8.7.76	0
NS7	W.H.Fox Terrier	6 6/12	M	cystitis	8.7.76	7

M : Male F : Female

TABLE 56

PROPORTION OF ANAGEN HAIR

Group Five. Dogs with hormonal disorders (12)

No.	Breed	Age (Years)	Sex	Disorder	Date of Examination	Percentage of hair in Anagen
OH2	Irish setter	3	M	S.C.T.	21.7.78	5
OH8	W.H.White	8	F	iatrogenic Cushings	17.3.77	83
OH9	Pekinese	13	F	Cushing-like syndrome	11.11.76	0
OH15	pug	6	F	hair loss	4.4.77	0
OH16	W.H.White	4	M	alopecia	28.12.76	89
OH17	W.H.White	4 10/12	F	dermatitis & acanthosis	21.3.77	89
OH20	collie	9 6/12	F	hair loss & epidermitis	7.7.78	0
OH21	Labrador	5	Fn	Alopecia	10.11.77	0
OH25	Terrier	8	M	un-diagnosed	22.10.76	34
OH27	Spaniel	4	F	hair loss & epidermitis	26.1.77	0
OH30	Labrador	1 6/12	Mn	hair loss	29.1.77	0
OH37	Scottish T.	5 6/12	F	alopecia & over weight	3.3.77	45

M : Male Mn : neutered male F : female
Fn : neutered female

TABLE 57

PROPORTION OF ANAGEN HAIR

Group Six. Dogs with pyoderma (16)

No.	Breed	Age (years)	Sex	Date of Examination	Percentage hair in Anagen
P1	C.Spaniel	5	F	7.3.77	5
P6	W.H.White	8 4/12	M	28.12.76	94
P9	Terrier	8	M	10.2.77	16
P10	B.Collie	1 3/12	M	5.11.76	0
P13	Cairn	6	M	17.2.77	81
P14	Alsatian	3	M	4.11.76	0
P17	Lurcher	6/12	M	29.10.76	0
P18	Boxer	5 6/12	M	17.11.76	0
P19	Old English Sheepdog	3	M	25.11.76	85
P22	Pyrenean Mountain Dog	3	M	19.1.77	1
P48	W.H.White	8	M	27.7.76	73
P58	W.H.White	9 9/12	M	11.3.77	70
P61	Labrador	4 3/12	F	8.7.77	0
P64	Collie	4 6/12	M	24.1.77	3
P72	Labrador	3 6/12	F	8.11.76	6
P100	Labrador			7.1.77	10

M : Male F : Female

TABLE 58

PROPORTION OF ANAGEN HAIR

Group Seven. Dogs with allergic conditions affecting the skin (3)

No.	Breed	Age (years)	Sex	Date of Examination	Percentage hair in Anagen
A1	Collie	5 6/12	Fn	3.5.77	10
A10	Doberman	5 6/12	M	24.2.77	0
A18	Golden Retriever	3/12	F	5.11.76	1

M : Male Fn : Neutered female

TABLE 59

PROPORTION OF ANAGEN HAIR

Group Eight. Dogs with ectoparasitic disorders (9)

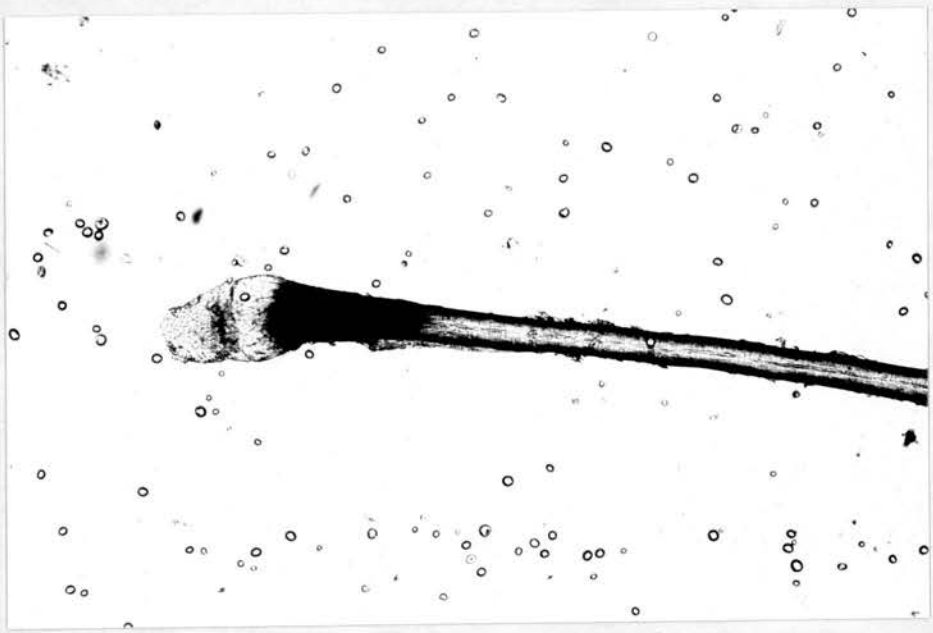
No.	Breed	Age (years)	Sex	Disorder	Date of Examination	Percentage hair in Anagen
E1	Shitzu	1 8/12	M	mange d.	14.12.76	100
E2	Dachshund	3 6/12	F	mange d.	30.12.76	7
E3	Cairn	9	F	mange d.	26.11.76	100
E6	Labrador-x	1	F	mange d.	30.11.76	6
E7	K.Chas.Span.	10weeks	F	mange s.	9.11.76	2
E23	Boxer	3/12	M	mange s.	10.1.77	0
E29	Scottish T.	2 6/12	F	mange d.	5.7.76	38
E32	Retriever	1 4/12	M	fleas	17.2.77	15
E34	Beagle	3	M	fleas	2.11.76	0

mange d. : demodectic mange

mange s. : sarcoptic mange

Figure 2. Hair in anagen, well defined, expanded root. Pigment present in shaft (x 70)

Figure 3. Hair in anagen stage showing well defined, expanded root (x 170)



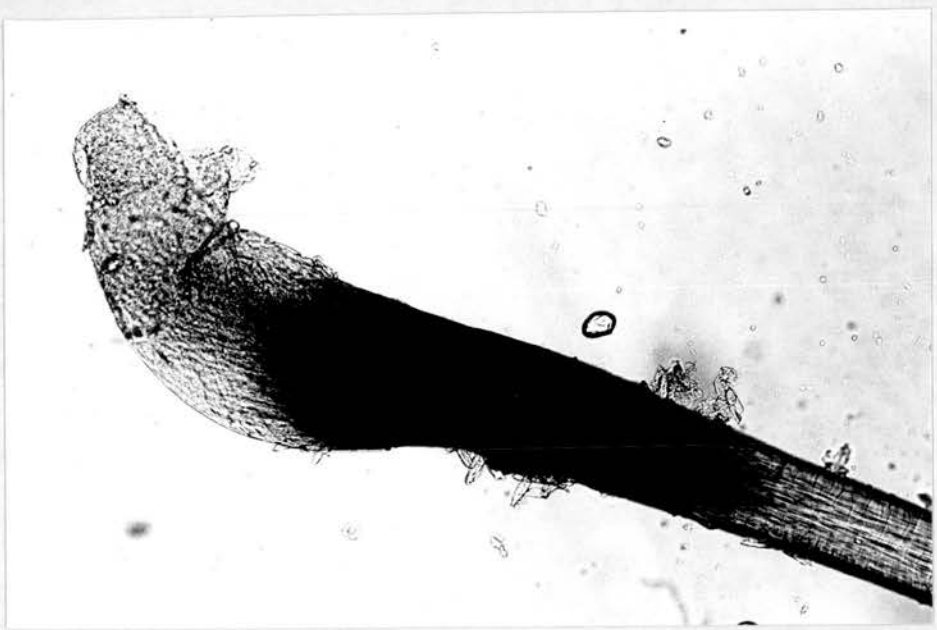
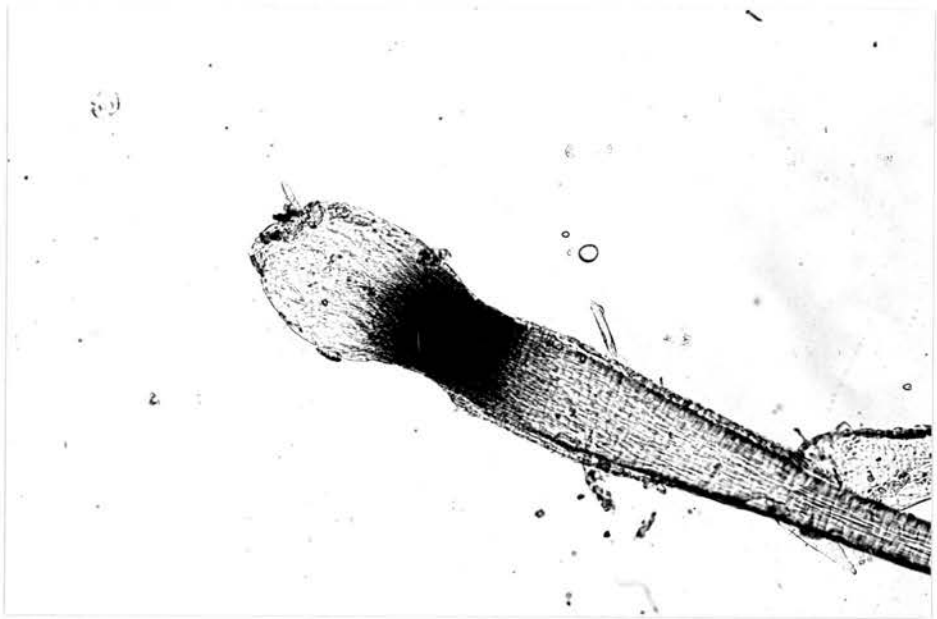


Figure 4. Hair in metanagen showing early constriction of hair bulb, part of root sheath still showing

Figure 5. Hair in telogen, keratinised debris round root, little pigment in the shaft (x 170)



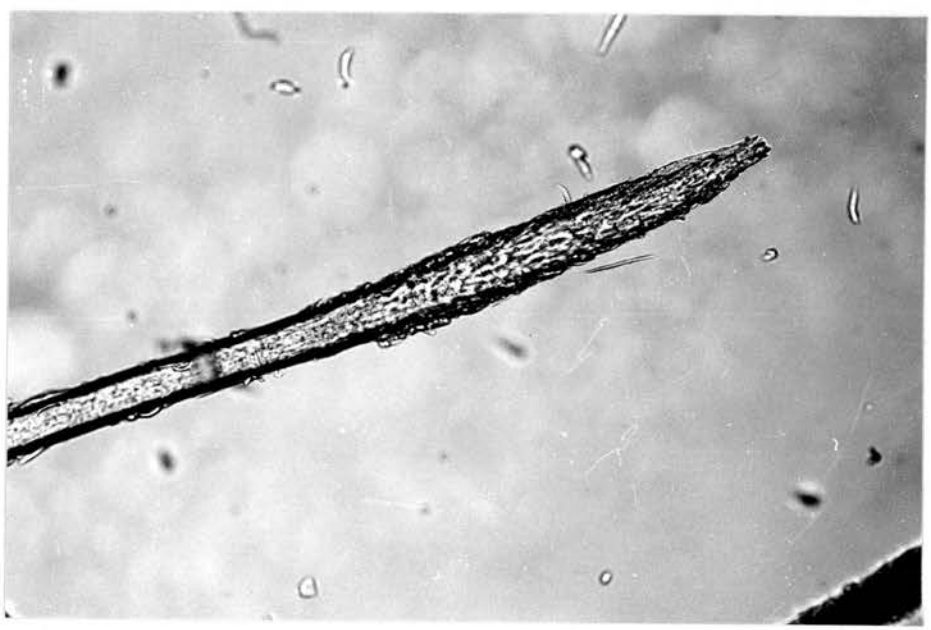
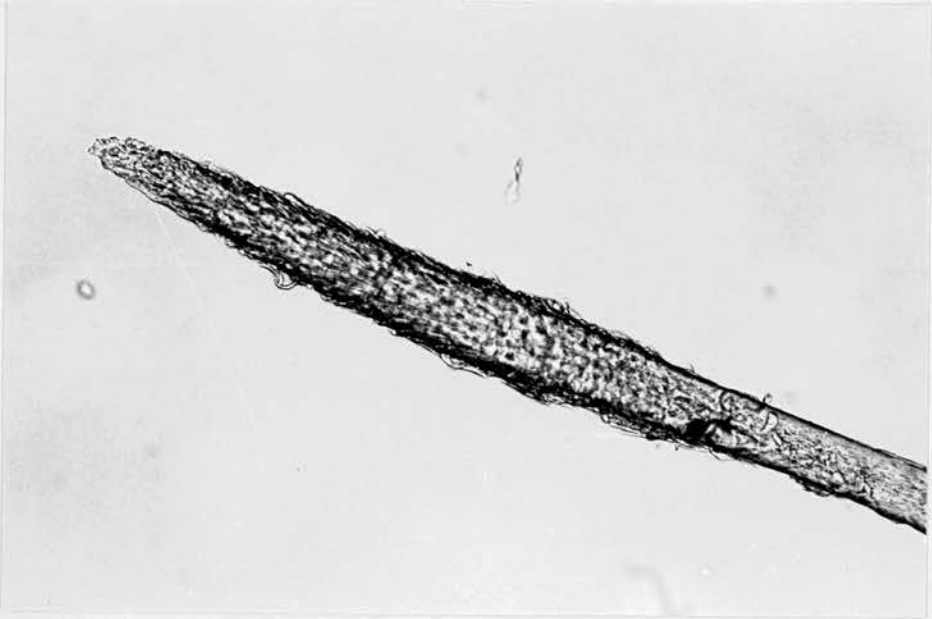


Figure 6. Hair in telogen, keratinised debris round root, absence of pigment in the shaft (x 170)

Figure 7. Hairs in telogen, lack of pigment in shaft, debris around root, root shrunken, commencement of "club" (x 70)



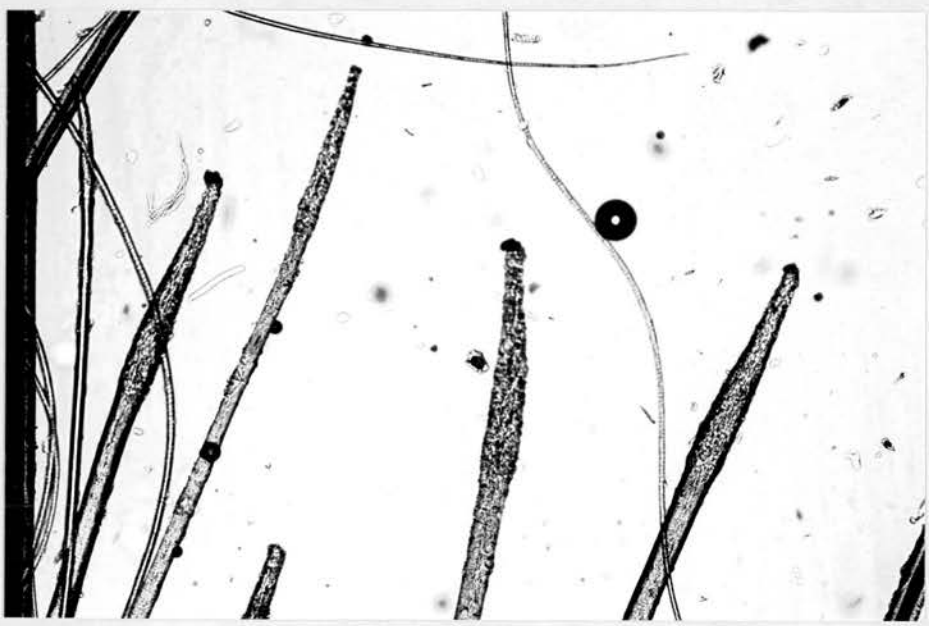
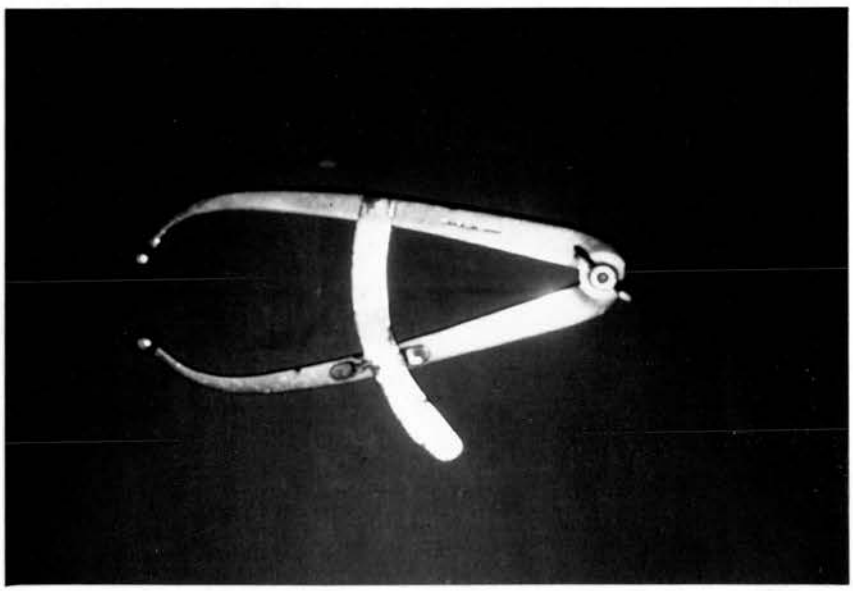


Figure 8. Callipers used for measuring skin thickness



ILLUSTRATIONS OF CLINICAL CASES

The following figures illustrate the appearance of certain dogs of Group HS and indicate the nature and the condition of the skin and the distribution of skin and coat change before and during treatment. Brief details are given for each case.

Figure 12. Case HS2, Poodle, M, 12 y.o., sparse hair, slight detmatitis

Figure 13. Case HS2, sparse hair, pustules and scaliness

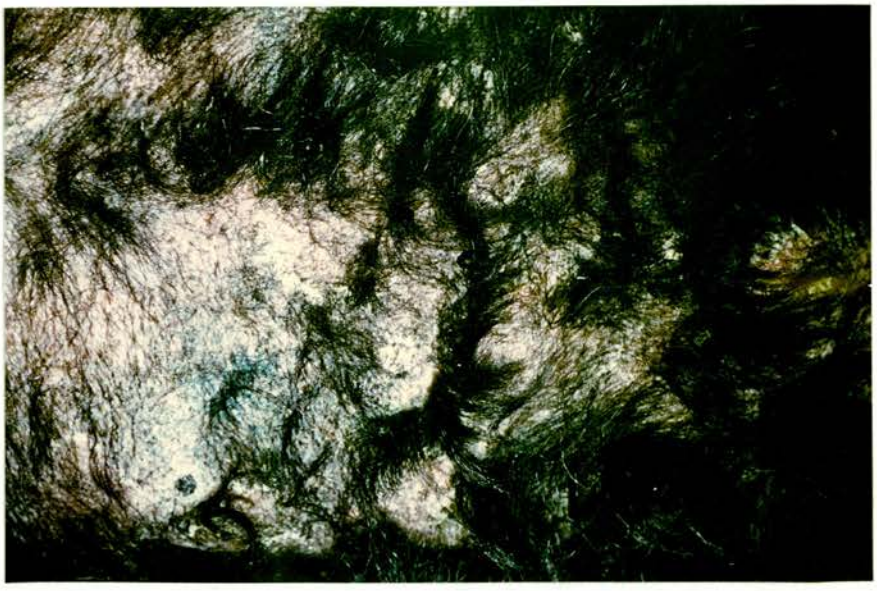


Figure 14. Case HS2, areas of alopecia with pigmentation and scaliness, sparse hair

Figure 15. Case HS2, alopecia, tenting of skin, some erythema

Figure 16. Case HS5, Labrador, F, 3 y.o.
Alopecia and sparse hair, left flank, before treatment

Figure 17. Case HS5, area of alopecia
and sparse hair reduced following treatment

Figure 18. Case HS7, Dachshund, F, 7 6/12 y.o., ventral surface, hair sparse, skin pigmented, before treatment

Figure 19. Case HS7, Alopecia of ear, sparse hair on shoulder, before treatment

Figure 20. Case HS7, Alopecia ventral aspect tail and perineal region, sparse coat posterior thighs, pigmentation of skin, before treatment

Figure 21. Case HS7, ventral surface, commencement of hair growth, during treatment

Figure 22. Case HS7, reduction in pigmentation, hair growth progressing, during treatment

Figure 23. Case HS7, general hair growth, improvement in coat quality, reduction in pigmentation, during treatment

Figure 24. Case HS22, Yorkshire Terrier, M, 3 y.o., marked alopecia of left hind leg and flank, upperpart, before treatment

Figure 25. Case HS22, Alopecia of breast, shoulder and upper part of forelegs and of upper part of hind legs, (bilaterally symmetrical) during treatment

Figure 26. HS22, Good hair growth during treatment

Figure 27. Case HS9, Poodle, M, 10 y.o., sparse hair, pigmentation of neck, withers and shoulder, before treatment

Figure 28. Case HS9, sparse hair, pigmentation of withers, before treatment

Figure 29. Case HS9, pigmentation still present, some new growth of hair, during treatment

Figure 30. Case HS9, some new hair growth in neck region, during treatment

Figure 31. Case HS9, new hair growth laterally, slow hair growth on neck, left side. The dog has lost weight during treatment

Figure 32. Case HS9, same dog as figure above. Hair growth on right side is slower, pigmentation still evident; during treatment

Figure 33. Case HS9, slow hair growth, skin pigmentation persists, during treatment

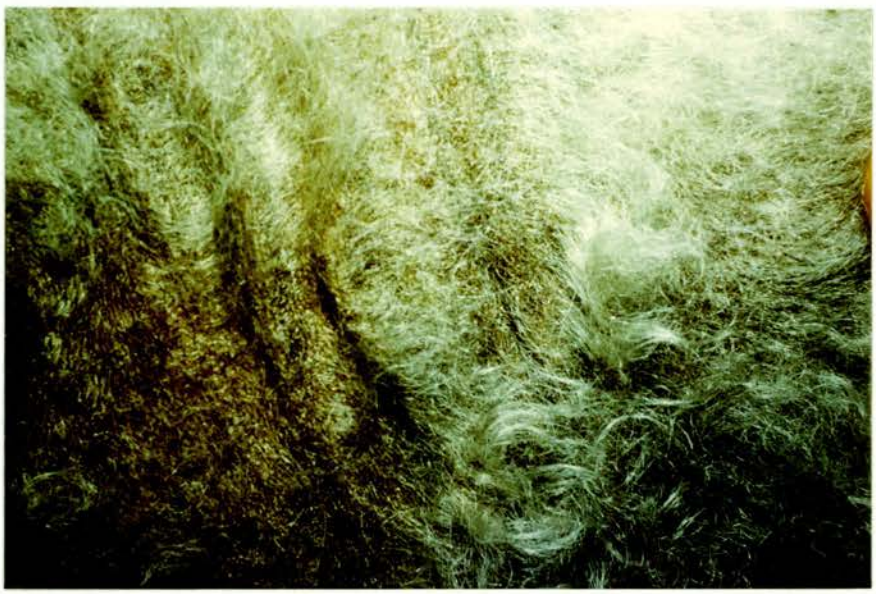


Figure 34. Case HS13, Airedale, M, 10 y.o. extensive alopecia dorsally and laterally, skin pigmentation well marked, before treatment

Figure 35. Case HS13, alopecia, pustules, erythema and pigmentation, before treatment

Figure 36. Case HS13, hair growth has started on former area of alopecia, during treatment

Figure 37. Case HS13, hair growth active, small area of alopecia remains on left sub-lumbar area, during treatment

Figure 38. Case HS13, regression of hair growth following cessation of treatment

Figure 39. Case HS13, close up of above

Figure 40. Case HS13, extensive, well-marked alopecia and pigmentation following cessation of treatment

Figure 41. Case HS25, Airedele, F, bilaterally symmetrical alopecia of lumbar and flank regions, sparse coat on rest of back; pigmentation is more marked laterally, before treatment

Figure 42. Case HS35, Lakeland Terrier, F, 12 y.o., marked ventral alopecia, some pigmentation, before treatment

Figure 43. Case HS35, alopecia, severe pigmentation in sacral region

PROTEIN BOUND IODINE AND TOTAL IODINE VALUES IN SERUM

The results of serum PBI and TI assay are recorded in Tables 60 , 61 , 62 , 63 , 64 and 65 for Group N, HS, OH, P, A and EP respectively. Table 66 gives the results of assays before and after treatment had started for Group HS. The results may be summarised as follows.

Group	Range PBI (mcg/100ml)	Mean ± Standard Deviation PBI (mcg/100ml)	Range TI (mcg/100ml)
N	1.0 - 6.0	3.18 ± 1.63	7.5 - mt 15
HSX	0.5 - 7.7	4.08 ± 2.11	3.0 - mt 20
HSY	0.5 - 11.7	4.52 ± 2.61	3.0 - mt 20
OH	1.4 - 4.7	2.98 ± 1.29	5.7 - mt 15
P	0.25- 10.5	2.33 ± 2.62	3.0 - mt 20
A	1.0 - 7.5	3.60 ± 2.77	5.5 - mt 20
EP	1.0 - 7.5	3.78 ± 2.29	5.0 - mt 15

HSX: before treatment HSY: after treatment had started
mt: more than

An analysis of variance of results for PBI (variance ratio 1.82) failed to show any statistically significant difference between the groups.

Table 60

Group N, serum protein bound iodine (PBI) and total iodine (TI) values in normal dogs at time of first examination

Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)	Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)
N8	2.0	9.0	N29	6.0	8.5
N15	4.5	8.0	N30	3.0	9.0
N21	3.5	mt 15	N31	1.5	mt 15
N23	2.0	12.0	N33	1.0	12.5
N26	4.5	11.0	N34	5.0	13.0
N28	2.0	7.5			

Table 61

Group HS, serum protein bound iodine (PBI) and total iodine (TI) values in dogs with suspected hypothyroidism at time of first examination

Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)	Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)
HS2	0.5	5.0	HS24	5.8	
HS6	5.0	mt 20	HS25	6.5	mt 15
HS8	4.5	7.8	HS26	4.5	mt 20
HS11	2.0	4.0	HS28	2.0	7.5
HS13	5.0	13.0	HS29	6.5	9.0
HS19	3.5		HS30	2.5	mt 20
HS21	1.0	3.0	HS31	0.0	13.5
HS22	4.5		HS33	2.2	4.5
HS23	7.7	mt 15	HS35	2.0	4.0

Table 62

Group OH, serum protein bound iodine (PBI) and total iodine (TI) values in dogs with other hormonal conditions

Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)	Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)
OH8	1.9	9.5	OH25	4.5	
OH9	1.5	14.7	OH27	4.5	10.2
OH15	4.0	mt 15	OH33	4.0	mt 15
OH16	1.5	5.7	OH37	3.5	
OH17	1.4		OH37	2.5	12.5
OH19	3.0	12.3	OH37	3.8	5.5
			OH37	4.7	7.2

mt: more than

Table 63

Group P, serum protein bound iodine (PBI) and total iodine (TI) values in dogs with pyoderma

Dog No.	PBI (mcg/100ml)		TI (mcg/100ml)	Dog No.	PBI (mcg/100ml)		TI (mcg/100ml)
P1	0.25		3.0	P15	4.0		9.0
P1	1.5		4.0	P17	5.5		8.5
P2	4.0		9.5	P19	5.0	mt	15
P3	5.0		8.0	P21	4.0	mt	20
P5	1.5		18.0	P21	1.8	mt	20
P6	2.2		3.0	P23	1.0	mt	15
P7	6.5		13	P31	7.5	mt	20
P8	9.2	mt	15	P58	1.8		1.8
P9	3.3		9.0	P64	6.0	mt	15
P10	6.0			P65	1.5		
P10	1.0		4.0	P65	4.0		
P10	9.5	mt	15	P65	2.7		13.5
P11	3.0		11.5	P72	2.5		
P12	5.0		7.0	P72	7.0		12.5
P14	4.5			P72	4.9		8.0

Table 64

Group A, serum protein bound iodine (PBI) and total iodine (TI) values in dogs with allergic disorders at time of first examination

Dog No.	PBI (mcg/100ml)		TI (mcg/100ml)	Dog No.	PBI (mcg/100ml)		TI (mcg/100ml)
A12	3.5		5.5	A33	5.0	mt	20
A17	1.0	mt	20	A40	1.0	mt	15
A18	7.5	mt	15				

Table 65

Group EP, serum protein bound iodine (PBI) and total iodine (TI) values in dogs with external parasitism at time of first examination

Dog No.	(mcg/100ml)		(mcg/100ml)	Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)
EP1	7.5	mt	15	EP32	4.7	
EP3	1.0		5.0	EP33	1.8	5.5
EP7	2.0		5.0	EP43	5.0	15.0
EP22	4.5		12			

mt: more than

Table 66

Group HS, serum protein bound iodine (PBI) and total iodine (TI) values before and after commencement of treatment

Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)	Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)
HS2			HS11		
before	0.5	5.0	before	2.0	4.0
after	6.5	10.0	after	6.5	
	2.0	8.5		4.1	mt 15
		12.0		5.5	13.5
	1.0	10.0		3.2	10.0
	4.7	9.0		4.2	14.0
	2.4	5.0		3.0	mt 20
	2.5	15		1.7	13.0
	1.5	mt 20		5.1	12.2
	3.25				
	3.0	3.0	HS13		
	4.0		before	5.0	13.0
	3.0	14.5	after	5.0	mt 15
	7.5	mt 15		6.0	16
	3.7	mt 15		9.0	mt 20
				6.0	mt 20
HS6				6.7	mt 20
before	5.0	mt 20		6.7	mt 20
	3.2	mt 20		5.0	mt 15
	3.0	mt 15			
	1.0	mt 20	HS22		
after	7.7	mt 15	before	4.5	
	3.2	mt 15	after	3.5	12.0
	3.0	mt 15		2.5	15.0
HS8			HS23		
before	4.5	7.8	before	7.7	mt 15
after	3.0	4.0		2.0	12.0
	5.2	8.2		5.5	mt 15
	0.8	6.0	after	11.5	
	4.8	12.0		4.0	mt 20
	0.5	8.5		5.0	mt 15
	4.6			7.5	
	4.5	7.5		7.0	11
	5.0	14.5		9.0	
	6.0	10.0		11.7	
	5.5	7.7			
	1.0	8.5	HS24		
			before	5.8	
HS10			after	3.5	6.5
before				3.0	6.5
after	5.1	11.0		6.7	9.7
	4.6			1.5	11.5
	5.5	mt 20		2.0	4.7
	9.5	mt 20		4.2	6.0

mt: more than

Table 66 (contd.)

Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)	Dog No.	PBI (mcg/100ml)	TI (mcg/100ml)
HS25			HS35		
before	6.5	mt 15	before	0.0	4.0
after	3.5	18.0	after	2.0	13.0
	2.0	11.5		4.5	4.0
	1.2	4.5		2.5	3.0
	5.5	15.0		2.5	3.0
				3.0	10.0
HS26					
before	4.5	mt 20			
	2.0	8.0			
after	2.0	15.0			
	1.8	12.0			
HS28					
before	2.0	7.5			
after	4.5				
	3.75				
	2.0	7.5			
HS29					
before	6.5	9.0			
	6.1	7.0			
after	1.0	15.0			
	1.2	14.5			
	1.5	12.0			
	1.2	mt 15			
	1.7	10.5			
	1.0	12.5			
HS30					
before	2.5				
	7.5	mt 20			
	5.25				
HS33					
before	2.2	4.5			
	1.0	6.7			
after	2.1	4.0			
	7.0				
	9.0	12.3			
	3.6	mt 15			
	1.0	4.5			

mt: more than

SERUM CHOLESTEROL VALUES

Normal Dogs (Group N)

Cholesterol values obtained from the first samples taken from the group as a whole are presented in Table 67. For the 68 dogs the values ranged from 1.59 to 10.93 mmol/l. The mean and standard deviation were 5.25 ± 1.85 mmol/l.

Experiment 1

Cholesterol values for the 17 dogs were obtained from serum collected 2 hours before and 2 hours after feeding and are recorded in Table 68. For the first sample the range was 3.24 - 7.25 mmol/l, mean and SD were 4.79 ± 1.16 and the standard error of the mean was 0.28. For the second sample, the range was 2.58 - 7.58 mmol/l, mean and standard deviation were 4.63 ± 1.36 and the standard error of the mean was 0.33.

The paired 't' test was conducted with the following result:

No. of pairs	Mean differences	't'
17	0.165	0.992

There is no significant difference between the pre- and post-prandial serum cholesterol levels.

Experiment 2

The individual cholesterol values are presented in

Table 67

Group N: Cholesterol values of first blood sample from normal dogs

Dog No.	Cholesterol (mmol/l)	Dog No.	Cholesterol (mmol/l)
N1	1.59	N35	3.51
N2	4.01	N36	4.82
N3	4.13	N37	1.99
N4	6.89	N38	2.18
N5	3.03	N39	4.17
N6	3.72	N40	9.34
N7	6.20	N41	10.93
N8	3.70	N42	6.67
N9	6.11	N43	4.50
N10	6.25	N44	9.67
N11	7.24	N45	8.00
N12	3.55	N46	5.50
N13	4.82	N47	5.34
N14	4.85	N48	6.67
N15	5.82	N49	4.67
N16	4.36	N50	6.83
N17	2.58	N51	4.68
N18	4.84	N52	4.68
N19	2.95	N53	7.75
N20	4.84	N54	8.40
N21	6.15	N55	7.60
N22	2.76	N56	5.17
N23	3.80	N57	3.76
N24	4.56	N58	5.49
N25	7.90	N59	4.39
N26	4.48	N60	4.39
N27	6.21	N61	6.74
N28	5.50	N62	4.52
N29	4.53	N63	6.14
N30	3.45	N64	5.34
N31	3.24	N65	5.52
N32	3.45	N66	7.92
N33	4.48	N67	7.29
N34	5.18	N68	5.93

No. 68
Mean: 5.25
SD: $\pm$ 1.85
Range: 1.59 - 10.93

Table 68

Experiment 1, serum cholesterol values (mmol/l) in normal dogs, two hours before and two hours after feeding

Dog No.	Before feeding	After feeding
N10	6.25	5.82
N11	7.24	7.58
N12	3.55	4.34
N13	4.82	5.17
N14	4.85	4.82
N15	4.34	4.48
N21	6.15	6.90
N23	3.80	3.44
N26	4.48	3.45
N27	6.21	4.49
N28	5.50	6.21
N29	4.49	4.53
N30	3.45	3.45
N31	3.24	3.10
N32	3.45	2.58
N33	4.48	3.80
N34	5.18	4.52
No. 17		
Mean	4.79	4.63
Standard deviation	1.16	1.36
Standard error	0.28	0.33

Table 69. Immediately after the 7 dogs were fed, the range, mean and SD and standard error of the mean were 2.58 - 6.89 mmol/l, 4.51 ± 1.56 and 0.59 respectively. Two hours after feeding the results were 2.57 to 7.23 mmol/l, 4.76 ± 1.72 and 0.65. Nineteen hours after feeding, they were (for 5 dogs) 2.24 - 6.54 mmol/l, 4.64 ± 1.73 and 0.77.

The paired 't' test was applied to the results of samples 1 and 2 and to samples 1 and 3:

	No. of pairs	Mean differences	't'
Samples 1 & 2	7	0.257	0.907
Samples 1 & 3	5	0.336	2.403

There were no significant differences between the serum cholesterol values.

Experiment 3

The individual cholesterol values are presented in Table 70. Table 70 also gives the mean, standard deviation and standard error of the mean for the values at each of the 7 times of sampling.

Table 71 sets out the results of the 't' test. There were no significant differences in the cholesterol values between the various pairs at times of sampling.

Experiment 4

The individual serum cholesterol values obtained at the 8 samplings are presented in Table 72, which also

Table 69

Experiment 2, serum cholesterol values (mmol/l) in normal dogs, immediately after and two and four hours after feeding

Dog No.	Time after feeding		
	Immediately	2 hours	19 hours
Time	day 1, 2.15 pm	day 1, 4 pm	day 2, 9 am
N4	6.89	7.23	6.54
N8	3.70	5.18	na
N17	2.58	2.91	2.24
N19	2.95	2.57	na
N23	4.68	3.83	3.96
N36	4.82	5.55	4.40
N68	5.93	6.08	6.08
No.	7	7	5
Mean	4.51	4.76	4.64
Standard deviation	1.56	1.72	1.73
Standard error	0.59	0.65	0.77

na: not available

Table 70

Experiment 3, serum cholesterol values (mmol/l) in normal dogs, on seven occasions during two days

Dog		DAY 1				DAY 2		
	Sample No.	1	2	3	4	5	6	7
	Time of sampling	9 am	noon	2.15pm	5 pm	9 am	noon	4 pm
N5		3.03	2.58	2.76	2.85	3.10	2.87	2.98
N6		2.43	2.58	2.58	3.06	2.90	2.74	3.34
N9		6.11	6.20	6.59	6.13	6.65	5.69	6.28
N15		4.52	3.79	3.22	-	3.87	3.55	4.51
N16		4.36	4.50	4.50	4.48	3.71	3.87	3.95
N17		2.58	2.43	2.50	2.42	2.01	2.15	1.93
N23		3.55	2.98	2.51	2.91	2.75	6.62	3.39
N24		4.56	5.17	5.51	-	4.34	5.17	5.00
N		8	8	8	6	8	8	8
Mean		3.89	3.78	3.77	3.64	3.67	4.08	3.92
Standard deviation		1.24	1.40	1.58	1.41	1.41	1.58	1.34
Standard error		0.44	0.49	0.56	0.57	0.50	0.56	0.47

Table 71

Experiment 3: significance of differences between serum cholesterol values of different blood samples, 't' test

Comparison Samples no.	No. of pairs	Mean differences	't'
1 and 6	8	0.190	0.425
2 and 6	8	0.304	0.621
3 and 6	8	0.311	0.553
4 and 6	6	0.348	0.514
5 and 6	8	0.416	0.793
1 and 7	8	0.030	0.174
2 and 7	8	0.144	0.792
3 and 7	8	0.151	0.576
4 and 7	6	0.003	0.020
5 and 7	8	0.256	1.797

includes the mean and standard deviation and the standard error of the mean for each group of samples.

The results of the 't' test are set out in Table There were no significant differences between sets of samples compared.

Experiment 5

The individual serum cholesterol values obtained at the 6 samplings are presented in Table 74, , with the mean and SD and the standard error of the mean. The results of the 't' test are set out in Table 75. . There were no significant differences between the groups of samples.

Dogs with Suspected Hypothyroidism (Group HS)

Serum cholesterol values estimated for these dogs at the time of first examination are presented in Table 76 and Table 77 for the subgroups HSU and HST respectively. The results of later cholesterol estimations are given in Tables 78 and 79.

At the time of first examination, the serum cholesterol values for the 35 HSU dogs ranged from 4.06 - 14.01 mmol/l, with mean and standard deviation of 8.51 $\pm$ 2.44 mmol/l. For the 12 HST dogs, the range was 2.96 - 12.72 mmol/l, 6.51 $\pm$ 2.99 mmol/l (mean $\pm$ SD).

Dogs with Other Hormonal Disorders (Group OH)

The results of serum cholesterol estimation are

Table 72

Experiment 4, serum cholesterol values (m mol/l) in normal dogs, at intervals before and after feeding. Dogs were fed daily at 2 pm.

Dog	Sample No.	1	2	3	4	5	6	7	8
		5 hrs before	3 hrs before	Imm. after	3 hrs after	5 hrs before	2 hrs before	Imm. after	2 hrs after
	Time	9 am	11 am	2.15	5pm	9 am	11 am	2.15	4 pm
N2		4.01	2.84	3.67	3.20	3.56	3.44	4.17	4.00
N3		4.13	5.44	5.17	5.27	4.59	5.34	4.50	4.28
N17		2.77	2.92	2.92	2.75	2.75	2.95	2.95	na
N25		7.90	8.96	8.61	7.20	6.34	6.89	7.34	6.89
N		4	4	4	4	4	4	4	3
Mean		4.70	5.04	5.09	4.61	4.31	4.65	4.74	5.06
St. deviation		2.22	2.88	2.53	2.05	1.55	1.81	1.86	1.59
St. error		1.11	1.44	1.26	1.02	0.77	0.91	0.93	0.92

before and after refer to before and after feeding

na: not available

st: standard

Imm: immediately

Table 73

Experiment 4: Significance of differences between serum cholesterol values of different blood samples, 't' test

Comparison Samples no.	No. of pairs	Mean differences	't'
1 and 3	4	0.390	1.279
2 and 3	4	0.053	0.195
3 and 5	4	0.487	1.483
5 and 7	4	0.430	1.806
6 and 7	4	0.085	0.248
7 and 8	3	0.280	3.248

Table 74

Experiment 5, serum cholesterol values (m mol/l) in normal dogs immediately before and at intervals after feeding. Dogs fed at 9 am on Day 1

Dog Sample No.	1	2	3	4	5	6
	Imm. before	2 hrs after	4 hrs after	6 hrs after	8 hrs after	24 hrs after
Time	8.45am	11am	1 pm	3 pm	5 pm	9 am
N1	1.59	1.89	2.24	2.92	2.65	2.00
N15	3.95	3.39	3.55	3.39	3.06	3.23
N17	2.75	2.42	2.91	2.42	2.42	2.24
N20	4.84	4.10	4.23	4.57	4.03	4.33
N23	7.86	7.32	5.49	5.25	4.74	5.05
N34	5.50	6.66	6.29	6.29	na	na
N	6	6	6	6	5	5
Mean	4.42	4.29	4.12	4.14	3.38	3.37
St. deviation	2.20	2.23	1.54	1.49	0.98	1.32
St. error	0.90	0.91	0.63	0.61	0.44	0.59

before and after refer to before and after feeding

na: not available

st: standard

imm: immediately

Table 75

Experiment 5: Significance of differences between serum cholesterol values of different blood samples, 't' test

Comparison Samples no.	No. of pairs	Mean differences	't'
1 and 2	6	0.118	0.401
1 and 3	6	0.297	0.628
1 and 4	6	0.275	0.495
1 and 5	5	0.872	1.211
1 and 6	5	0.828	1.554

Table 76

Group HS, Serum cholesterol values in previously untreated (HSU) dogs with suspected hypothyroidism, single sample

Dog No.	Cholesterol (mmol/l)	Dog No.	Cholesterol (mmol/l)
HS1	8.21	HS25	5.55
HS2	8.68	HS26	9.07
HS3	6.14	HS27	9.66
HS4	4.99	HS28	6.80
HS5	7.76	HS29	8.14
HS6	9.42	HS30	8.49
HS7	11.20	HS32	4.06
HS8	8.97	HS33	7.95
HS9	11.37	HS34	9.04
HS11	6.56	HS36	8.06
HS14	8.50	HS38	4.98
HS16	6.46	HS39	12.06
HS18	7.02	HS40	9.23
HS20	4.82	HS41	8.51
HS21	11.68	HS43	12.75
HS22	8.28	HS44	13.55
HS23	7.25	HS45	8.86
HS24	14.01		

n = 35 mean: 8.51 mmol/l

SD: $\pm$ 2.44

Table 77

Group HS: Serum cholesterol values in previously treated (HST) dogs with suspected hypothyroidism, single sample

Dog No.	Cholesterol (m mol/l)
HS10	6.48
HS12	5.17
HS13	7.43
HS15	4.52
HS17	6.20
HS19	2.96
HS31	6.70
HS35	11.90
HS37	12.72
HS42	5.47
HS46	3.79
HS47	4.82

n = 12 mean: 6.51 mmol/l

SD: $\pm$ 2.99

Table 78

Group HSU, serum cholesterol values of previously untreated cases of suspected hypothyroidism

Dog No. HS1

Dates sampled	Cholesterol (mmol/l)
24. 8.78	8.21

Dog No. HS2

Dates sampled	Cholesterol (m mol/l)
2.11.76	8.68
15.11.76	5.19
25.11.76	8.98
13.12.76	7.59
10. 1.77	5.51
24. 1.77	7.31
7. 2.77	9.30
14. 2.77	7.45
28. 2.77	6.03
21. 3.77	7.12
4. 4.77	8.51
25. 4.77	6.19
16. 5.77	8.86
26. 5.77	5.92
12. 7.77	6.77
26. 7.77	6.13
16. 8.77	7.20
6. 9.77	7.65
6.10.77	7.44
13.10.77	5.17
22.11.77	7.10
22.12.77	6.55
24. 1.78	9.37
7. 2.78	7.88
18. 4.78	8.10
31. 5.78	4.48
20. 6.78	5.49
18. 7.78	5.17

Dog No. HS3

Dates sampled	Cholesterol (m mol/l)
6. 6.78	6.14
23. 6.78	3.60
6. 7.78	4.50
18. 7.78	4.03
31. 8.78	6.56
28. 9.78	5.33

Dog No. HS4

Dates sampled	Cholesterol (mmol/l)
14.11.77	4.99
16.11.77	4.36
4.12.77	4.99
28. 2.78	4.13
18. 4.78	3.76
16. 5.78	6.85
27. 6.78	4.52
8. 8.78	3.79
31. 8.78	5.34

Dog No. HS5

Dates sampled	Cholesterol (m mol/l)
29. 6.78	7.76
20. 7.78	4.96
15. 8.78	4.14
28. 9.78	4.56
20.11.78	4.99
26. 3.79	2.66
28. 5.79	7.23

Dog No. HS6

Dates sampled	Cholesterol (m mol/l)
24. 6.77	9.42
1. 7.77	7.94
11. 7.77	9.51
25. 7.77	6.56
2. 8.77	6.89
15. 8.77	6.31
15. 9.77	5.00
15.11.77	4.52
16. 1.78	6.13
15. 3.78	8.61
21. 4.78	5.49
25. 5.78	4.26
21. 7.78	4.84
7. 8.78	5.33
4. 9.78	7.67
6.11.78	5.36
18. 1.79	3.88
12. 6.79	4.35

Dog No. HS7

Dates sampled	Cholesterol (mmol/l)
9. 3.78	11.20
15. 3.78	11.71
22. 3.78	12.06
24. 4.78	9.56
17. 5.78	11.03
17. 5.78	10.68
15. 6.78	12.20
15. 6.78	8.89
14. 7.78	10.17
14. 8.78	9.69
28. 9.78	13.38
31.10.78	14.47
29.11.78	12.33
12. 1.79	10.80
28. 2.79	11.40
28. 3.79	11.03
15. 6.79	11.96

Dog No. HS8

Dates sampled	Cholesterol (m mol/l)
12. 1.77	8.97
5. 2.77	6.20
14. 2.77	6.91
19. 2.77	6.95
14. 3.77	6.03
21. 3.77	6.22
4. 4.77	6.56
22. 4.77	7.93
6. 5.77	9.25
20. 5.77	9.37
3. 6.77	8.09
18. 7.77	5.54
19. 8.77	7.75
17.10.77	6.78
17.11.77	7.27
16. 2.78	7.00
24. 4.78	7.76
26. 6.78	9.37
30. 6.78	8.80
23.10.78	9.61
23.11.78	10.01
5. 3.79	9.33

Table 78 (contd.)

Dog No. HS9

Dates sampled	Cholesterol (mmol/l)
22. 8.77	11.37
25. 8.77	7.24
8. 9.77	9.65
22. 9.77	8.21
6.10.77	7.24
13.10.77	8.72
20.10.77	8.40
3.11.77	7.75
24.11.77	7.76
9. 2.78	9.35
23. 2.78	6.69
23. 3.78	6.08
25. 4.78	5.40
28. 4.78	4.25
28. 4.78	5.47
1. 6.78	4.68
29. 6.78	6.72
18. 8.78	6.08
7. 3.79	6.03

Dog No. HS11

Dates sampled	Cholesterol (mmol/l)
13.12.76	6.56
17. 2.77	8.42
2. 3.77	8.51
17. 3.77	8.14
29. 3.77	9.39
12. 4.77	8.88
10. 5.77	7.41
26. 5.77	8.14
28. 7.77	6.48
1.12.77	5.86
13. 2.78	8.90
27. 2.78	6.54

Dog No. HS14

Dates sampled	Cholesterol (mmol/l)
26.11.76	8.50
4. 4.78	5.28
4. 5.78	7.08
11. 5.78	7.24
27. 6.78	6.46
20. 2.79	8.20
20. 3.79	7.56
8. 5.79	6.20
3. 7.79	5.17

Dog No. HS16

Dates sampled	Cholesterol (mmol/l)
11. 5.78	6.46
25. 5.78	4.26

Dog No. HS18

Dates sampled	Cholesterol (mmol/l)
18. 1.77	7.02
28. 1.77	8.28
15.11.77	6.46
29. 3.78	6.03
30. 6.78	3.10
28. 9.78	6.77

Dog No. HS20

Dates sampled	Cholesterol (mmol/l)
30. 3.78	4.82
27. 4.78	10.68
25. 5.78	7.13

Dog No. HS21

Dates sampled	Cholesterol (mmol/l)
11.11.76	11.68
30.12.76	8.28
20. 1.77	7.24

Dog No. HS22

Dates sampled	Cholesterol (mmol/l)
8.12.76	8.28
21.12.76	3.66
4. 2.77	3.58
11. 2.77	4.53
3. 3.77	4.07
1. 4.77	5.50
4. 5.77	4.07
19. 8.77	4.20
4.11.77	2.45
11.11.77	3.99

Dog No. HS23

Dates sampled	Cholesterol (mmol/l)
29.11.76	7.25

Dog No. HS23 (contd.)

Dates sampled	Cholesterol (mmol/l)
3.12.76	5.82
17. 1.77	6.46
27. 1.77	5.52
3. 2.77	6.46
11. 2.77	6.80
17. 2.77	4.86
3. 3.77	3.80
17. 3.77	4.81
21. 4.77	6.55
3. 6.77	5.83
26. 9.77	5.17

Dog No. HS24

Dates sampled	Cholesterol (mmol/l)
4.11.76	14.01
22.11.76	11.10
6.12.76	9.06
20.12.76	9.71
11. 1.77	7.77
17. 2.77	7.77
24. 2.77	9.04

Dog No. HS25

Dates sampled	Cholesterol (mmol/l)
23.11.76	5.55
2.12.76	4.49
10. 1.77	4.97
11. 2.77	5.50
25. 2.77	6.54
25. 3.77	5.33
25. 4.77	5.33

Dog No. HS26

Dates sampled	Cholesterol (mmol/l)
15. 2.77	9.07
1. 3.77	11.39
14. 3.77	7.93
28. 3.77	9.71

Table 78 (contd.)

Dog No. HS27

Dates sampled	Cholesterol (mmol/l)
21. 7.77	9.66
22. 7.77	7.82
2. 8.77	3.77
16. 8.77	4.80
9.10.77	7.23
23. 3.78	6.08

Dog No. HS28

Dates sampled	Cholesterol (mmol/l)
18. 2.77	6.80
3. 3.77	4.48
11. 3.77	3.05
5. 4.77	5.32

Dog No. HS29

Dates sampled	Cholesterol (mmol/l)
2. 3.77	8.14
14. 3.77	8.61
21. 3.77	9.10
4. 4.77	8.14
19. 4.77	7.94
3. 5.77	7.77
9. 6.77	8.68
5. 8.77	7.58
8.11.77	9.48

Dog No. HS30

Dates sampled	Cholesterol (mmol/l)
28. 2.77	8.49
15. 3.77	6.91
4. 4.77	9.25
12. 4.77	9.25
26. 4.77	10.01
16. 6.77	7.77
15. 8.77	7.16
24.10.77	5.90

Dog No. HS32

Dates sampled	Cholesterol (mmol/l)
19. 9.78	4.06
27. 9.78	3.92

Dog No. HS33

Dates sampled	Cholesterol (mmol/l)
10.11.76	7.95
5. 1.77	5.18
24. 1.77	5.53
29. 1.77	5.17
5. 2.77	6.55
14. 2.77	6.56
5. 3.77	5.17
2. 4.77	6.90
28. 5.77	5.89
6. 8.77	8.75
5.11.77	5.67
23.11.77	5.49
3. 3.78	7.93
8. 5.78	10.81
20. 5.78	6.78
5. 6.78	5.69

Dog No. HS34

Dates sampled	Cholesterol (mmol/l)
7.11.77	9.04
11.11.77	7.99

Dog No. HS36

Dates sampled	Cholesterol (mmol/l)
11. 9.78	8.06
19. 9.78	6.20
10.10.78	7.76

Dog No. HS38

Dates sampled	Cholesterol (mmol/l)
4.12.78	4.98
10. 1.79	14.60
30. 1.79	4.24
27. 2.79	4.25
3. 4.79	7.43
5. 6.79	3.79

Dog No. HS39

Dates sampled	Cholesterol (mmol/l)
15. 2.79	12.06
16. 2.79	12.53

Dog No. HS39 (contd.)

Dates sampled	Cholesterol (mmol/l)
17. 2.79	12.93
5. 3.79	13.38
19. 3.79	12.06
30. 3.79	8.81
23. 4.79	9.69
7. 5.79	9.12

Dog No. HS40

Dates sampled	Cholesterol (mmol/l)
13. 2.79	9.23

Dog No. HS41

Dates sampled	Cholesterol (mmol/l)
6. 3.79	8.51
19. 3.79	9.13
30. 3.79	8.51
23. 4.79	8.40
7. 5.79	7.00

Dog No. HS43

Dates sampled	Cholesterol (mmol/l)
6. 6.79	12.75

Dog No. HS44

Dates sampled	Cholesterol (mmol/l)
28. 5.79	13.55
30. 5.79	12.16
6. 6.79	12.41

Dog No. HS45

Dates sampled	Cholesterol (mmol/l)
1. 6.79	8.86

Table 79

Group HST, serum cholesterol values of previously treated cases of suspected hypothyroidism

Dog No. HST10

Dates sampled	Cholesterol (mmol/l)
10. 2.77	6.48
17. 2.77	7.12
24. 2.77	5.54
9. 3.77	6.56
28. 3.77	7.40
7. 5.77	5.17
30. 5.77	6.27
21. 7.77	7.39
1. 9.77	8.15
24. 9.77	11.85
8.10.77	6.46
22.10.77	5.82
11.11.77	5.49
21. 1.78	5.57
18. 3.78	6.88
15. 7.78	6.83
16. 8.78	5.65
25.10.78	5.51
13.12.78	3.87
27. 1.79	2.90
17. 7.79	9.37

Dog No. HST12

Dates sampled	Cholesterol (mmol/l)
10. 7.78	5.17
20.10.78	4.23
1. 2.79	7.52

Dog No. HST13

Dates sampled	Cholesterol (mmol/l)
31. 3.77	7.43
14. 4.77	8.41
21. 4.77	8.62
5. 5.77	10.70
17. 5.77	9.96
3. 6.77	10.36
4. 7.77	8.35
4. 8.77	8.32
5. 9.77	7.38
10.11.77	5.17
20. 3.78	6.30

Dog No. HST 13 (contd.)

Dates sampled	Cholesterol (mmol/l)
24. 6.78	7.35
16.10.78	13.89
27.10.78	12.41
5. 3.79	16.80
9. 7.79	12.16

Dog No. HST15

Dates sampled	Cholesterol (mmol/l)
18. 7.78	4.52

Dog No. HST17

Dates sampled	Cholesterol (mmol/l)
29. 6.78	6.2

Dog No. HST19

Dates sampled	Cholesterol (mmol/l)
14. 3.77	2.96
2. 6.77	4.14
26. 8.77	5.81
19.12.77	5.48
17. 1.78	6.46
3. 2.78	5.86
3. 3.78	7.29
25. 4.78	5.64
9. 6.78	4.50
16. 1.79	4.82

Dog No. HST31

Dates sampled	Cholesterol (mmol/l)
1. 4.77	6.70
6. 7.77	6.48
10. 8.77	6.55
4.10.77	6.17
6.11.78	7.10

Dog No. HST35

Dates sampled	Cholesterol (mmol/l)
18. 3.77	11.90
1. 4.77	10.40
12. 4.77	11.84
26. 4.77	10.71
20. 5.77	8.40
2. 6.77	7.11
16. 6.77	7.45

Dog No. HST37

Dates sampled	Cholesterol (mmol/l)
14.11.78	12.72
27.11.78	13.34

Dog No. HST42

Dates sampled	Cholesterol (mmol/l)
19. 4.79	5.47

Dog No. HST46

Dates sampled	Cholesterol (mmol/l)
1. 5.79	3.79

Dog No. HST47

Dates sampled	Cholesterol (mmol/l)
1. 5.79	4.82
20. 6.79	5.78

presented in Table 80 , for samples taken at the first examination. The range was 2.67 - 13.44 mmol/l, with mean and standard deviation of 6.11 ± 2.05 mmol/l. The results of later assays are given in Table 81 .

Dogs with Non-Hormonal Skin Diseases (Group NH)

The serum cholesterol values in samples taken at the first clinical examination are presented in Tables 82 , 83 and 84 for Groups P, A and EP respectively and where later samples were assayed the results are presented in Tables 85, 86 and 87 respectively.

At the first examination, the range for Group P was 2.21 - 14.70 mmol/l, 5.61 ± 2.03 mmol/l (mean ± SD). For Group A it was 2.95 - 9.88 mmol/l, 5.82 ± 1.56 mmol/l (mean ± SD) and for Group EP it was 2.79 - 10.34 mmol/l, 5.10 ± 1.77 mmol/l (mean ± SD).

The results of cholesterol assay for all groups are illustrated in Figure 9.

Table 80

Group OH, first values of serum cholesterol from '47' dogs

Dog No.	Serum Cholesterol (mmol/l)	Dog No.	Serum Cholesterol (mmol/l)
OH 1	4.52	OH25	4.06
OH 2	7.10	OH26	4.83
OH 3	9.97	OH27	5.50
OH 4	7.32	OH28	7.59
OH 5	5.36	OH29	5.81
OH 6	6.46	OH30	6.19
OH 7	4.20	OH31	6.72
OH 8	6.38	OH32	6.19
OH 9	5.65	OH33	7.77
OH10	10.34	OH34	3.60
OH11	9.05	OH35	5.00
OH12	7.52	OH36	6.30
OH13	13.44	OH37	7.75
OH14	6.55	OH38	4.88
OH15	5.92	OH39	4.66
OH16	2.67	OH40	4.59
OH17	6.15	OH41	2.76
OH18	5.84	OH42	3.55
OH19	4.07	OH43	6.20
OH20	5.78	OH44	6.69
OH21	3.76	OH45	6.38
OH22	4.48	OH46	4.20
OH23	7.58	OH47	9.52
OH24	6.55		

No.	47
Mean	6.11 ± 2.05 (SD)
Range	$2.67 - 13.44$

Table 81

Group OH, serum cholesterol values in dogs with other hormonal disorders

Dog No. OH3

Dates sampled	Cholesterol (mmol/l)
2. 5.78	9.97
18. 5.78	7.24
4. 7.78	7.93

Dog No. OH6

Dates sampled	Cholesterol (mmol/l)
2. 6.78	6.46
5. 6.78	7.58

Dog No. OH8

Dates sampled	Cholesterol (mmol/l)
17. 3.77	6.38
26. 4.77	6.56
15. 9.77	4.69

Dog No. OH10

Dates sampled	Cholesterol (mmol/l)
11. 7.77	10.34
26. 7.77	16.50
28. 8.77	11.95
23. 9.77	15.80
28.10.77	15.83
16.12.77	15.19
31. 5.78	13.44
31. 5.78	14.99

Dog No. OH11

Dates sampled	Cholesterol (mmol/l)
17. 3.78	9.05
5. 4.78	5.78
4. 5.78	7.76
13. 6.78	7.39

Dog No. OH12

Dates sampled	Cholesterol (mmol/l)
14. 2.78	7.52
20. 6.78	8.72

Dog No. OH13

Dates sampled	Cholesterol (mmol/l)
22. 8.78	13.44
20. 9.78	13.78

Dog No. OH14

Dates sampled	Cholesterol (mmol/l)
14. 9.78	6.55
12.10.78	5.91

Dog No. OH16

Dates sampled	Cholesterol (mmol/l)
10.12.77	2.67
28.12.77	4.79
24. 3.77	4.53
25. 6.77	5.65

Dog No. OH17

Dates sampled	Cholesterol (mmol/l)
22. 3.77	6.15
26. 9.77	4.82
3. 3.78	5.86
1. 5.78	6.22
2. 6.78	4.20
20. 6.78	5.17

Dog No. OH18

Dates sampled	Cholesterol (mmol/l)
3.10.77	5.84
7.10.77	5.48
17.10.77	4.84
7.11.77	5.17

Dog No. OH21

Dates sampled	Cholesterol (mmol/l)
27.10.77	3.76
8.12.77	3.09

Dog No. OH23

Dates sampled	Cholesterol (mmol/l)
13. 7.78	7.58
15. 8.78	4.52
5. 9.78	4.13
17.10.78	5.01

Dog No. OH24

Dates sampled	Cholesterol (mmol/l)
13. 6.77	6.55
7. 7.77	7.38
18. 7.77	7.02

Dog No. OH26

Dates sampled	Cholesterol (mmol/l)
14. 2.77	4.83
31. 5.77	5.42

Dog No. OH27

Dates sampled	Cholesterol (mmol/l)
26. 1.77	5.50
13. 7.77	8.01
26. 7.77	7.43

Dog No. OH28

Dates sampled	Cholesterol (mmol/l)
14. 7.77	7.59
15. 8.77	9.19
4. 5.78	5.95
19. 5.78	7.43
31. 5.78	5.00

Table 81 (contd.)

Dog No. OH30	
Dates sampled	Cholesterol (mmol/l)
29. 1.77	6.19
12. 2.77	4.49

Dog No. OH31	
Dates sampled	Cholesterol (mmol/l)
11. 7.77	6.72
16. 8.77	4.77

Dog No. OH32	
Dates sampled	Cholesterol (mmol/l)
25. 3.77	6.19
28. 7.77	8.28
16. 8.77	7.20
27. 3.78	9.78
25. 4.78	7.94
2. 4.79	8.50

Dog No. OH36	
Dates sampled	Cholesterol (mmol/l)
10. 4.78	6.30
16.10.78	8.30
18. 6.78	6.73

Dog No. OH37	
Dates sampled	Cholesterol (mmol/l)
28. 2.77	7.75
4. 3.77	5.98
5. 3.77	6.80
11. 3.77	6.56
25. 3.77	6.88
28. 4.77	5.98
26. 5.77	6.21

Dog No. OH38	
Dates sampled	Cholesterol (mmol/l)
7. 3.79	4.88
15. 3.79	1.84

Dog No. OH39	
Dates sampled	Cholesterol (mmol/l)
6. 3.79	4.66
13. 3.79	3.55

Dog No. OH46	
Dates sampled	Cholesterol (mmol/l)
14. 5.79	4.20
3. 7.79	3.79

Table 82

Group P, serum cholesterol values at first examination of dogs with pyoderma

Dog No.	Cholesterol (mmol/l)	Dog No.	Cholesterol (mmol/l)	Dog No.	Cholesterol (mmol/l)
P1	7.01	P34	4.99	P81	6.65
P2	6.15	P35	7.00	P82	4.68
P3	3.11	P40	5.17	P83	4.68
P4	8.68	P41	4.99	P84	5.45
P5	5.47	P46	3.65	P85	4.52
P6	5.73	P47	2.39	P86	6.38
P7	4.48	P48	4.43	P87	6.20
P8	3.89	P49	4.37	P88	4.88
P9	5.83	P50	4.43	P89	14.70
P10	2.74	P51	3.45	P90	5.17
P11	2.59	P52	5.69	P91	3.34
P12	7.60	P53	5.91	P92	3.95
P13	4.86	P55	7.50	P93	7.59
P14	6.62	P56	6.56	P94	7.27
P15	5.87	P57	8.12	P95	5.65
P16	3.56	P58	3.66	P96	5.56
P17	3.45	P59	12.95	P97	2.41
P18	4.18	P60	7.12	P98	10.18
P19	7.40	P61	9.12	P99	4.14
P20	6.90	P62	6.20		
P21	6.22	P63	4.82		
P22	5.49	P64	4.81		
P23	6.22	P65	4.49		
P24	6.20	P66	2.21		
P25	6.14	P67	5.54		
P26	5.49	P68	5.49		
P27	5.17	P69	4.06		
P28	5.35	P70	5.68		
P29	6.50	P71	3.88		
P30	9.64	P72	5.17		
P31	5.53	P78	5.35		
P32	3.79	P79	5.17		
P33	5.47	P80	5.81		

No.	85
x	5.61 ± 2.03
Range	2.21 - 14.70

Table 83

Group A, serum cholesterol values at first examination of dogs with allergic skin conditions

Dog No.	Cholesterol (mmol/l)	Dog No.	Cholesterol (mmol/l)
A1	7.60	A29	4.00
A2	8.44	A30	7.47
A3	4.44	A31	6.46
A4	3.79	A32	8.55
A5	4.20	A33	6.22
A6	4.83	A34	6.72
A7	9.98	A35	6.08
A8	4.49	A36	4.52
A9	5.33	A37	7.96
A10	6.48	A38	5.67
A11	5.92	A40	6.80
A12	4.89	A41	5.53
A13	3.33	A42	4.54
A14	7.77	A44	5.00
A15	7.76	A45	6.20
A16	7.81	A46	5.17
A17	2.95	A47	3.62
A18	7.91	A48	7.38
A19	3.76	A49	6.20
A20	6.72	A50	4.53
A21	5.98	A51	5.17
A22	4.04	A52	6.99
A23	5.69	A53	5.73
A24	4.50	A54	5.17
A25	5.81	A55	5.54
A26	4.20	A56	8.27
A27	3.80	A57	5.33
A28	7.00		

No.	55
x	5.82 $\pm$ 1.56
Range	2.95 - 9.98

Table 84

Group EP, serum cholesterol values at first examination of dogs with external parasitism

Dog No.	Cholesterol (mmol/l)	Dog No.	Cholesterol (mmol/l)
EP1	3.80	EP23	8.68
EP2	4.14	EP29	3.32
EP3	7.25	EP30	4.17
EP4	4.34	EP31	5.86
EP5	5.54	EP32	4.53
EP6	5.17	EP33	5.18
EP7	4.53	EP34	8.09
EP8	4.11	EP35	4.11
EP9	6.66	EP36	9.56
EP11	5.11	EP37	3.60
EP12	3.79	EP38	6.88
EP13	10.34	EP39	5.48
EP14	6.78	EP40	4.82
EP15	3.10	EP41	4.26
EP16	3.62	EP42	4.35
EP17	4.85	EP43	4.06
EP18	3.34	EP44	3.22
EP19	2.79	EP45	6.94
EP20	5.33	EP46	6.58
EP21	4.46	EP47	3.55
EP22	2.79	EP48	4.82
		EP49	5.68

No.	43
x	5.10 ± 1.77
Range	2.79 - 10.34

Table 85

Group P, serum cholesterol values in dogs affected with pyoderma, serial sampling

Dog No. P1

Dates sampled	Cholesterol (mmol/l)
24. 1.77	7.01
28. 2.77	5.17
19. 3.77	5.86

Dog No. P4

Dates sampled	Cholesterol (mmol/l)
15. 4.77	8.63
6.3.78	6.08

Dog No. P6

Dates sampled	Cholesterol (mmol/l)
8.12.76	5.73
7. 4.77	5.50

Dog No. P10

Dates sampled	Cholesterol (mmol/l)
8.11.76	2.74
15.11.76	11.36
19.11.76	4.14
4.12.76	3.88

Dog No. P21

Dates sampled	Cholesterol (mmol/l)
19. 5.77	6.22
10. 2.78	6.38
27. 2.78	7.24
1.11.78	5.17
1.11.78	5.85
1.11.78	5.85
18. 1.79	5.17

Dog No. P24

Dates sampled	Cholesterol (mmol/l)
28. 6.77	6.20

Dog. No. P24 (contd.)

Dates sampled	Cholesterol (mmol/l)
21. 4.78	4.84
19. 6.78	5.52

Dog No. P25

Dates sampled	Cholesterol (mmol/l)
25. 7.78	5.70
15. 8.78	6.14
5. 9.78	4.20
26.10.78	6.03

Dog No. P28

Dates sampled	Cholesterol (mmol/l)
25. 7.78	5.35
15. 8.78	5.81

Dog No. P30

Dates sampled	Cholesterol (mmol/l)
1. 8.77	9.64
20. 9.77	8.89
25.11.77	5.86

Dog No. P35

Dates sampled	Cholesterol (mmol/l)
9.12.77	5.85
20.12.77	7.00

Dog No. P46

Dates sampled	Cholesterol (mmol/l)
29. 3.76	3.65
13. 4.76	4.06
5. 5.76	2.91
20. 5.76	6.21

Dog No. P47

Dates sampled	Cholesterol (mmol/l)
27. 7.77	2.39
29. 7.77	5.17

Dog No. P51

Dates sampled	Cholesterol (mmol/l)
12.10.78	3.45
9.11.78	7.00
7.12.78	7.38
22. 1.79	7.34

Dog No. P52

Dates sampled	Cholesterol (mmol/l)
9.11.78	5.69
30.11.78	7.83
18. 1.79	6.78
3. 4.79	10.98

Dog No. P53

Dates sampled	Cholesterol (mmol/l)
16.11.78	5.19
7.12.78	8.40
19. 1.79	6.89

Dog No. P58

Dates sampled	Cholesterol (mmol/l)
12. 3.77	3.66
18. 1.78	4.88

Dog No. P59

Dates sampled	Cholesterol (mmol/l)
23. 9.77	12.95
29. 9.77	6.64
24.10.77	5.53

Table 85 (contd.)

Dog No. P60

Dates sampled	Cholesterol (mmol/l)
29. 3.77	7.12
17. 6.77	5.17
18. 4.78	6.24

Dog No. P61

Dates sampled	Cholesterol (mmol/l)
24. 6.77	9.12 (
24. 6.77	9.12 (
8. 7.77	8.41
18. 7.77	6.87
2. 2.79	5.51

Dog No. P65

Dates sampled	Cholesterol (mmol/l)
24. 2.77	4.49
4. 4.77	6.22
9. 8.78	4.82

Dog No. P70

Dates sampled	Cholesterol (mmol/l)
21. 8.78	5.68
7. 9.78	4.10

Dog No. P71

Dates sampled	Cholesterol (mmol/l)
19. 4.78	3.88
17. 5.78	4.14

Dog No. P72

Dates sampled	Cholesterol (mmol/l)
9.11.76	5.17
26. 1.77	5.18
16. 2.77	4.49

Dog No. P78

Dates sampled	Cholesterol (mmol/l)
11.12.78	5.35
13. 3.79	13.41
19. 4.79	7.15

Dog No. P80

Dates sampled	Cholesterol (mmol/l)
25. 1.79	5.81
	9.69

Dog No. P82

Dates sampled	Cholesterol (mmol/l)
22. 1.79	4.68
27. 2.79	8.72

Dog No. P83

Dates sampled	Cholesterol (mmol/l)
19. 3.79	4.68
16. 4.79	8.72
14. 5.79	6.46

Dog No. P87

Dates sampled	Cholesterol (mmol/l)
8. 1.77	6.20
8. 5.79	8.53

Dog No. P94

Dates sampled	Cholesterol (mmol/l)
29. 3.79	7.27
16. 4.79	8.08

Dog No. P98

Dates sampled	Cholesterol (mmol/l)
1. 5.79	10.18
5. 6.79	7.24

Table 86

Group A, serum cholesterol values in dogs with allergic skin conditions, serial sampling

Dog No. A1

Dates sampled	Cholesterol (mmol/l)
26. 4.77	7.60
10.10.77	7.79

Dog No. A2

Dates sampled	Cholesterol (mmol/l)
6. 9.77	8.44
23. 9.77	6.15

Dog No. A3

Dates sampled	Cholesterol (mmol/l)
27. 5.77	4.44
7.11.78	3.51

Dog No. A7

Dates sampled	Cholesterol (mmol/l)
12. 5.78	9.98
26. 5.78	6.20

Dog No. A8

Dates sampled	Cholesterol (mmol/l)
19. 5.77	4.49
2. 6.77	4.38
19. 8.77	4.39

Dog No. A9

Dates sampled	Cholesterol (mmol/l)
6. 7.77	5.53
19.10.77	5.99

Dog No. A13

Dates sampled	Cholesterol (mmol/l)
6. 6.77	3.33
2. 6.78	4.52

Dog No. A14

Dates sampled	Cholesterol (mmol/l)
1. 6.77	7.77
8. 6.77	6.20

Dog No. A16

Dates sampled	Cholesterol (mmol/l)
17. 6.77	7.81
24. 6.77	7.90
	7.60

Dog No. A19

Dates sampled	Cholesterol (mmol/l)
27.10.77	3.76
31.10.77	5.00

Dog No. A22

Dates sampled	Cholesterol (mmol/l)
15. 8.78	4.04
12. 9.78	5.17

Dog No. A23

Dates sampled	Cholesterol (mmol/l)
8. 6.78	5.69
11. 6.78	7.84

Dog No. A24

Dates sampled	Cholesterol (mmol/l)
22. 6.78	4.50
13. 7.78	5.58

Dog No. A25

Dates sampled	Cholesterol (mmol/l)
2.11.77	9.21
30. 5.78	5.81
27. 6.78	6.69

Dog No. A26

Dates sampled	Cholesterol (mmol/l)
18. 5.78	4.20
20. 6.78	7.24

Dog No. A30

Dates sampled	Cholesterol (mmol/l)
7. 9.77	7.47
3. 3.78	11.25
25. 5.78	7.15

Dog No. A34

Dates sampled	Cholesterol (mmol/l)
1. 6.78	6.72
13. 6.78	4.80

Dog No. A36

Dates sampled	Cholesterol (mmol/l)
1. 5.78	4.52
11. 5.78	4.31
30. 5.78	5.17

Dog No. A45

Dates sampled	Cholesterol (mmol/l)
21. 9.78	6.20
24.10.78	11.15
20.11.78	6.06

Dog No. A46

Dates sampled	Cholesterol (mmol/l)
14.11.78	5.17
27.11.78	6.46

Dog No. A48

Dates sampled	Cholesterol (mmol/l)
16.11.78	7.38
7.12.78	6.09

Table 86 (contd.)

Dog No. A51

Dates sampled	Cholesterol (mmol/l)
19. 5.78	5.17
6. 6.78	4.84

Dog No. A54

Dates sampled	Cholesterol (mmol/l)
15.11.77	5.17
6.12.77	4.86

Dog No. A56

Dates sampled	Cholesterol (mmol/l)
21. 9.78	8.27
12.10.78	3.96

Table 87

Group EP, serum cholesterol values in dogs affected with external parasitism, serial sampling

Dog No. PE4

Dates sampled	Cholesterol (mmol/l)
20. 6.77	4.34
9. 3.78	4.48
26. 5.78	5.17

Dog No. PE8

Dates sampled	Cholesterol (mmol/l)
10. 1.77	4.11
21. 7.77	3.06

Dog No. PE9

Dates sampled	Cholesterol (mmol/l)
10. 1.77	6.66
6. 2.77	7.75
26. 6.78	5.71

Dog No. PE15

Dates sampled	Cholesterol (mmol/l)
20. 7.78	3.10
15. 8.78	2.59
5. 9.78	2.41

Dog No. PE23

Dates sampled	Cholesterol (mmol/l)
10. 1.77	8.68
22. 2.77	5.50
21. 7.77	4.25

Dog No. PE30

Dates sampled	Cholesterol (mmol/l)
23. 1.78	4.17
16. 6.78	4.52

Dog No. PE34

Dates sampled	Cholesterol (mmol/l)
22. 2.77	8.09
10. 3.78	7.43

Dog. No. PE36

Dates sampled	Cholesterol (mmol/l)
9. 8.77	9.56
19. 8.77	10.01
27. 3.78	6.39

Dog No. PE38

12.10.77	6.88
28.10.77	3.23

Dog No. PE40

Dates sampled	Cholesterol (mmol/l)
8. 6.78	4.82
7. 9.78	4.28

Dog No. PE45

22. 2.79	6.94
15. 3.79	10.15

Dog No. PE46

12. 3.79	6.58
16. 4.79	8.67

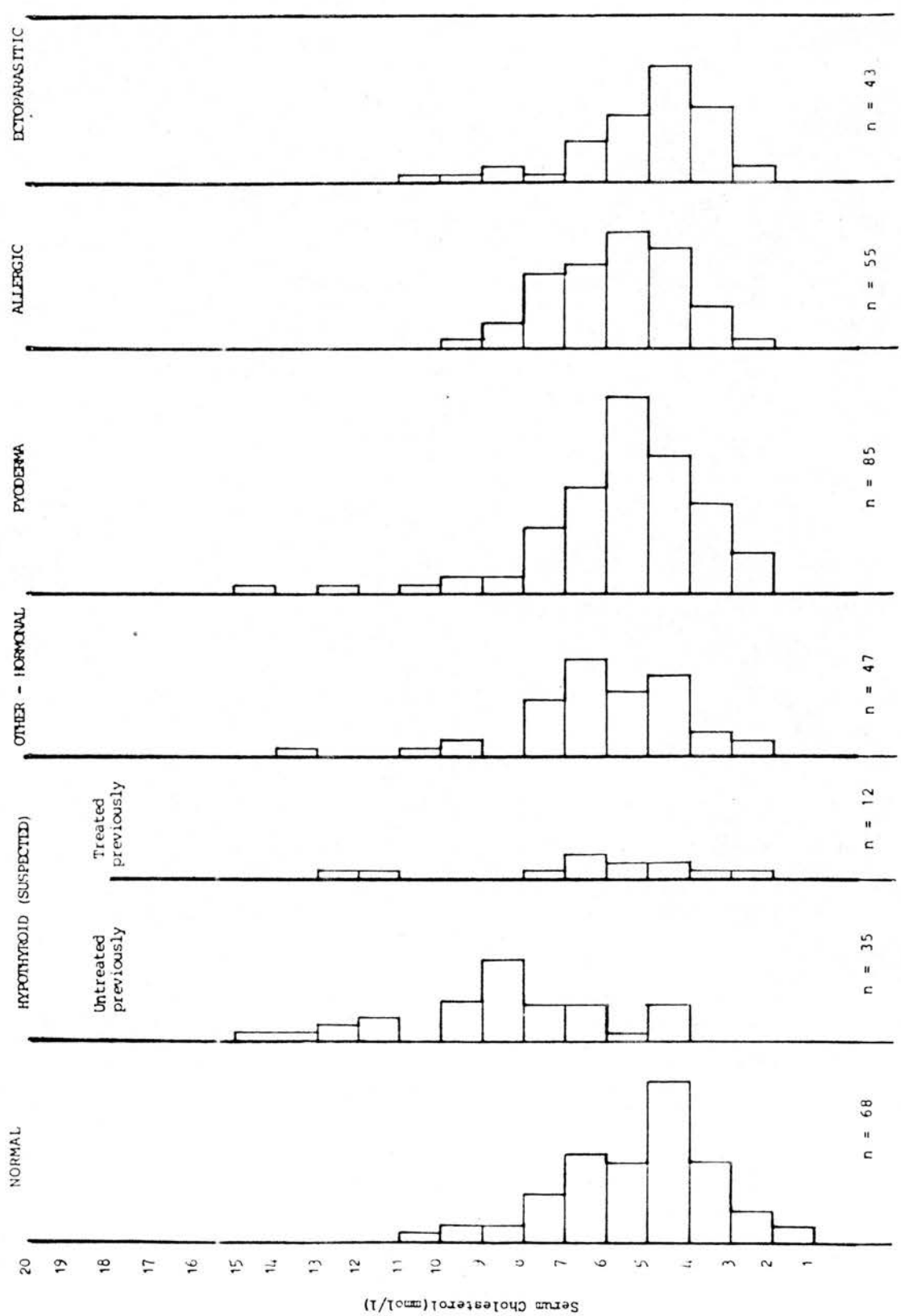


Figure 9.
Comparative distribution of serum cholesterol values in different dogs at time of first examination

SERUM THYROXINE VALUES

Group N, Normal Dogs

The serum thyroxine values obtained by T4RIA on blood samples taken at the time of first examination of 62 of the 68 dogs in this group are set out in Table 88 . The range of first values was 0.6 - 4.6 mcg/100ml, 2.20 ± 1.09 mcg/100ml (mean ± SD) i.e. in SI units, 7.72 - 59.20 nmol/l, 28.31 ± 14.03 (m ± SD).

For 66 of the dogs one or more assays were made starting at either the first or a subsequent clinical examination. The results are recorded in Table 89 , which also gives the mean and standard deviation of the values for each dog, when more than one value was obtained. As different numbers of T4RIA were conducted on different dogs, the results are quoted here as the range of the means, i.e. 0.6 - 4.7 mcg/100ml, 2.19 ± 1.07 mcg/100ml (mean ± SD). In SI units this is 7.22 - 60.49 nmol/l, 28.19 ± 13.77 nmol/l (mean ± SD).

The results of the 5 experiments were as follows.

Experiment 1

The results of serum T4RIA on blood obtained 2 hours before and 2 hours after feeding, of 9 dogs, are presented together with the mean, standard deviation and standard error in Table 90. No significant difference was found between the pre- and post-prandial T4 values when the paired 't' test was applied.

Table 88

Normal dogs, values of serum T4 and T3 obtained in blood samples taken at time of first examination

Dog No.	T4 (mcg/100ml)	T3 (ng/ml)	Dog No.	T4 (mcg/100ml)	T3 (ng/ml)
N1	1.05	0.90	N35	1.90	2.30
N2	1.40	0.90	N36	1.00	1.60
N3	2.20	1.00	N37	2.60	2.40
N4	2.60	1.65	N38	0.60	0.80
N5	1.35	1.10	N39	2.80	1.50
N6	1.00	1.15	N40	1.85	2.40
N7	1.50		N41	4.60	2.25
N8	0.60	1.70	N42	2.40	1.75
N9	2.20	1.50	N43	0.60	0.90
N10	3.80	3.70	N44	1.80	1.50
N11	2.80	0.95	N45	4.30	2.55
N12	2.80	1.50	N46	2.90	2.25
N13	3.00	1.00	N47	3.60	1.00
N14	4.00	1.80	N48	2.00	1.80
N15	4.00	2.85	N49	2.90	2.00
N16	2.60	1.20	N50	4.00	2.40
N17	1.00	0.95	N51	0.90	1.40
N18	2.60	1.45	N52	1.50	0.90
N19	2.30	0.95	N53	3.80	2.60
N20		0.50	N54	3.10	0.95
N21			N55		
N22	2.10	1.00	N56		
N23	0.95	1.00	N57	0.80	1.45
N24	1.65	1.20	N58	3.80	3.50
N25	1.60	1.40	N59	3.10	3.40
N26	1.50	1.40	N60	3.00	2.60
N27			N61	4.00	2.90
N28	2.10	1.55	N62	0.60	0.95
N29	2.60	1.75	N63	1.35	0.80
N30	0.90	1.65	N64	2.00	0.90
N31	1.20	1.75	N65	3.00	
N32	0.85	1.10	N66	2.80	1.45
N33		0.50	N67	2.80	2.70
N34	0.80	0.72	N68	1.20	0.40

	n: 62		n: 62
T4	mean: 2.20	T3	mean: 1.58
	SD: 1.09		SD: 0.76
	Range: 0.6 - 4.60		Range: 0.40 - 3.70

Table 89

Group N, serum T3 and T4 values in normal dogs

Dog No.	Date of sample	T3 (ng/ml)	T4 (mcg/100ml)	Dog No.	Date of sample	T3 (ng/ml)	T4 (mcg/100ml)
N1	30. 8.78	0.90	1.05	N6	18. 7.78	2.30	3.40
	30. 8.78	0.65	1.05	(ctd)	18. 7.78	1.65	3.20
	30. 8.78	1.45			18. 7.78	0.72	1.80
	30. 8.78	0.55	1.30		18. 7.78	0.80	0.40
	30. 8.78	0.65	1.60		19. 7.78	1.05	0.20
	31. 8.78	0.65	1.30		19. 7.78	1.45	3.10
					19. 7.78	1.50	0.30
N2	10. 8.78	0.90	1.40				
	10. 8.78	2.30	1.20	N7			1.50
	10. 8.78	0.80	0.85				
	10. 8.78	0.90	1.60	N8	22.11.76	1.70	0.60
	11. 8.78	0.72	1.60				
	11. 8.78	0.85	1.00	N9	13. 7.78	1.50	2.20
	11. 8.78		1.60		14. 7.78	1.35	3.00
	11. 8.78	0.90	1.10				
	11. 8.78	1.05		N10	11. 7.78	3.70	3.80
					11. 7.78	2.50	3.40
N3	9. 8.78	1.00	2.20				
	9. 8.78	2.30	2.40	N11	4. 7.78	0.95	2.80
	9. 8.78	1.25	3.40		4. 7.78	0.90	2.60
	9. 8.78	1.15	3.90				
	10. 8.78	1.05	2.00	N12	6. 7.78	1.50	2.80
	10. 8.78	0.85	1.00		6. 7.78	1.05	2.00
	10. 8.78	1.05	1.00				
	10. 8.78	1.25	2.80	N13	16. 6.78	1.00	3.00
					16. 6.78	2.00	2.40
N4	16. 6.78	1.65	2.60				
	16. 6.78	2.00	8.60	N14	26. 6.78	1.80	4.00
	16. 6.78	2.65	0.90		26. 6.78	1.75	4.20
N5	1. 8.78	1.10	1.35	N15	9.12.76	2.85	4.00
	1. 8.78	1.10	1.20		9.12.76	1.60	2.50
	1. 8.78	1.30	1.50		8. 6.77	1.15	2.10
	1. 8.78	1.00	0.95		8. 6.77	1.50	3.10
	2. 8.78	1.60	1.25		8. 6.77	1.65	1.20
	2. 8.78	1.45	1.60		8. 6.77	1.35	1.85
	2. 8.78	1.00	0.95		9. 6.77	1.35	2.10
					7. 2.78	1.15	0.60
N6	25. 1.78	1.15	1.00		7. 2.78	1.00	1.50
	25. 1.78	0.80	1.20		7. 2.78	1.45	0.60
	25. 1.78	0.90	1.20		7. 2.78	1.35	1.60
	25. 1.78	0.65	1.20		8. 2.78	1.35	1.80
	26. 1.78	0.75	1.40		15. 6.78	1.40	1.10
	26. 1.78	1.20	1.20		15. 6.78	1.35	1.00
	26. 1.78	1.20	1.85		16. 6.78	1.75	1.10
	26. 1.78	1.05	1.10		16. 6.78	1.75	2.60

Table 89 (contd.)

Dog No.	Date of sample	T3 (ng/ml)	T4 (mcg/100ml)	Dog No.	Date of sample	T3 (ng/ml)	T4 (mcg/100ml)
N15	28. 6.78	1.20	2.00	N20	7. 6.77	0.50	
(ctd)	28. 6.78	1.25	1.10		7. 6.77	0.65	1.40
	28. 6.78	1.55	2.60		7. 6.77	0.90	0.90
	28. 6.78	1.15	2.50		7. 6.77	0.65	0.95
	28. 6.78	1.75	1.20		7. 6.77	0.85	0.90
	28. 6.78	1.20	2.10		8. 6.77	0.50	0.60
N16	26. 6.78	1.20	2.60	N22	16. 5.78	1.00	2.10
	26. 6.78	1.75	3.40				
	26. 6.78	1.50	1.40	N23	26. 4.77	1.00	0.95
	27. 6.78	1.50	2.40		26. 4.77	1.55	0.60
	27. 6.78	1.50	3.20		4. 5.77	0.50	0.20
	27. 6.78	1.20	0.50		7. 6.77	1.10	2.00
	27. 6.78	1.20	2.40		7. 6.77	2.05	5.20
					7. 6.77	1.85	5.20
N17	26. 1.78	0.95	1.00		7. 6.77	2.00	3.20
	26. 1.78	0.95	0.80		7. 6.77	1.75	3.00
	26. 1.78	0.95	0.70		8. 6.77	1.65	1.90
	26. 1.78	1.25	0.65		16.11.77	1.20	0.60
	27. 1.78	1.00	0.95		16.11.77	1.20	0.60
	27. 1.78	1.50	1.20		16.11.77	1.15	0.65
	27. 1.78	1.20	0.60		16.11.78	1.15	0.60
	27. 1.78	1.20	0.70		17.11.78	1.15	0.60
	2. 2.78	1.25	1.15		17.11.78	1.55	1.20
	2. 2.78	1.20	1.40		17.11.78		4.30
	3. 2.78	1.20	1.10		2. 2.78	1.35	0.80
	29. 3.78	1.25	0.60		3. 2.78	1.20	0.80
	29. 3.78	1.55	1.00		2. 5.78	0.80	0.80
	29. 3.78	1.45	0.60				
	29. 3.78	1.10	2.20	N24	15. 3.78	1.20	1.65
	29. 3.78	1.65	1.80		15. 3.78	1.85	1.80
	30. 3.78	1.05	1.00		15. 3.78	1.65	2.60
	30. 3.78	1.85	1.20		16. 3.78	1.10	1.10
	30. 3.78	1.60	2.60		16. 3.78	0.72	1.40
	8. 6.78	0.80	0.70		16. 3.78	1.20	1.95
	19. 6.78	1.25	1.10				
	20. 6.78	0.72	0.60	N25	15. 3.78	1.40	1.60
	20. 6.78	1.20	1.00		15. 3.78	1.90	2.00
	20. 6.78	1.50	0.60		15. 3.78	1.40	2.00
	20. 6.78	1.20	1.00		16. 3.78	1.40	1.95
	21. 6.78	1.00	0.95		16. 3.78	1.20	2.55
	21. 6.78	1.20	1.40		16. 3.78	1.20	2.10
N18	2. 6.78	1.45	2.60	N26	1.12.76	1.40	1.50
N19	16.12.76	0.95	2.30	N28	12.11.76	1.55	2.10

Table 89 (contd)

Dog No.	Date of sample	T3 (ng/ml)	T4 (mcg/100ml)
N29	12.11.76	1.75	2.60
N30	15.12.76	1.65	0.90
N31	18.11.76	1.75	1.20
N32	26. 4.77	1.10	0.85
	26. 4.77	1.65	1.00
N33	1.12.76	0.50	
	1.12.76		1.20
N34	13. 1.77	0.72	0.80
	13. 1.77	1.15	1.00
	21. 1.77	1.00	0.80
N35	21. 7.77	2.30	1.90
N36	7. 2.79	1.00	1.60
	7. 2.79	0.95	3.00
	8. 2.79	1.30	1.20
N37	1. 3.79	2.40	2.60
N38	1. 3.79	0.80	0.60
N39	1. 3.79	1.50	2.80
N40	1. 3.79	2.40	1.85
N41	1. 3.79	2.25	4.60
	8. 3.79	1.75	4.80
N42	1. 3.79	1.75	2.40
N43	8. 3.79	0.90	0.60
N44	8. 3.79	1,50	1.80
N45	8. 3.79	2.55	4.30
N46	8. 3.79	2.25	2.90
N47	8. 3.79	1.00	3.60
N48	8. 3.79	1.80	2.00
N49	8. 3.79	2.00	2.90
N50	14. 3.79	2.40	4.00
N51	22. 3.79	1.40	0.90
N52	22. 3.79	0.90	1.50
N53	22. 3.79	2.60	3.80
N54	22. 3.79	0.95	3.10
N55	17. 4.79	2.50	3.00
N57	29. 3.79	1.45	0.80
N58	4. 4.79	3.50	3.80
N59	4. 4.79	3.40	3.10
N60	4. 4.79	2.60	3.00
N61	4. 4.79	2.90	4.00
N62	5. 4.79	0.95	0.60
N63	16. 4.79	0.80	1.35
N64	17. 4.79	0.90	2.00
N65			3.00
N66	25. 4.79	1.45	2.80
N67	27. 4.79	2.70	2.80
N68	27. 4.79	0.40	1.20
	27. 4.79	0.50	1.30
	27. 4.79	0.65	1.30

Table 89 (contd.)

Group N, serum T3 (ng/ml) and T4 (mcg/100ml) mean and standard deviation of values

Dog No.	T3		T4	
	Mean	SD	Mean	SD
N1	0.81	0.33	1.26	0.22
N2	1.05	0.51	1.29	0.30
N3	1.24	0.45	2.33	1.03
N4	2.10	0.50	4.03	3.30
N5	1.22	0.23	1.26	0.25
N6	1.14	0.43	1.50	0.98
N9	1.42	0.10	2.60	0.56
N10	3.10	0.85	3.60	0.28
N11	0.92	0.03	2.70	0.14
N12	1.27	0.32	2.40	0.56
N13	1.50	0.70	2.70	0.42
N14	1.77	0.03	4.10	0.14
N15	1.45	0.37	1.80	0.84
N16	1.40	0.21	2.27	1.01
N17	1.22	0.26	1.06	0.50
N20	0.67	0.17	0.95	0.28
N23	1.34	0.41	1.75	1.63
N24	1.28	0.40	1.75	0.51
N25	1.42	0.26	2.03	0.31
N32	1.37	0.40	0.93	0.10
N34	0.96	0.21	0.87	0.11
N36	1.08	0.20	1.93	0.95
N41	2.00	0.35	4.70	0.14
N68	0.52	0.12	1.27	0.05

Table 90

Experiment 1, serum T4 values (mcg/100ml) in normal dogs, 2 hours before and 2 hours after feeding

Dog No.	2 hours before feeding	2 hours after feeding
N10	3.80	3.40
N11	2.80	2.80
N12	2.80	2.00
N13	3.00	2.40
N14	4.00	4.20
N15	1.10	2.60
N23	0.95	0.60
N32	0.85	1.00
N34	0.80	1.00
No 9		
Mean	2.23	2.22
Standard deviation	1.31	1.20
Standard error	0.44	0.40

No of pairs	9
Mean difference	0.011
't'	0.049

Experiment 2

The results of serum T4RIA on samples obtained immediately after and 2 and 19 hours after feeding the dogs are recorded in Table 91 . When the paired 't' test was applied there were no significant differences in T4 values at the different times.

Experiment 3

The results are shown in Table 92 for samples assayed for T4 on 7 occasions during 2 days. When the data were arranged in pairs (Table 93), application of the 't' test revealed no significant differences.

Experiment 4

The results are set out in Table 94. A comparison of the differences, when the results obtained at different intervals are set out in pairs and subjected to the 't' test, shows no significant differences in serum T4 values at the various pre- and post-prandial intervals (Table 95).

Experiment 5

The results of T4RIA are given in Table 96 . The 't' test conducted on pairs of sets of assays failed to reveal any significant differences between the T4 values at the different intervals (Table 97).

Table 91

Experiment 2, serum T4 values (mcg/100ml) in normal dogs at intervals after feeding

Dog No.	Immediately after	2 hours after	19 hours after
N4	2.60	8.60	0.90
N17	1.15	1.40	1.10
N23	0.80	0.80	0.80
N36	1.50	3.00	1.20
N68	1.20	1.30	1.30
No.	5	5	5
Mean	1.45	3.02	1.06
Standard deviation	0.69	3.23	0.21
Standard error	0.31	1.44	0.09

Comparison:	No. of pairs	Mean difference	't'
Immediately after and 2 hours after	5	1.570	1.377
Immediately after and 19 hours after	5	0.390	1.167

Table 92

Experiment 3, serum T4 values (mcg/100ml) in normal dogs on seven occasions during two days

Dog No.	Sample No. / Time	1 9 am	2 noon	3 2.15pm	4 5pm	5 9am	6 noon	7 4pm
N5		1.35	1.20	1.50	0.95	1.25	1.60	0.95
N6		1.00	1.20	1.20	1.20	1.40	1.20	1.85
N15		0.60	1.50	0.60	1.60	1.80	1.10	1.10
N16		2.60	3.40	1.40	2.40	3.20	0.50	2.40
N17		1.00	0.80	0.70	0.65	0.95	1.20	0.60
N23		0.60	0.60	0.65	0.60	0.60	1.20	4.30
N24		1.65	1.80	2.60	1.10	1.40	na	1.95
N		7	7	7	7	7	6	7
Mean		1.26	1.50	1.24	1.21	1.51	1.13	1.88
Standard deviation		0.70	0.93	0.71	0.62	0.83	0.36	1.24
Standard error		0.27	0.35	0.27	0.23	0.31	0.14	0.47

na not available

Table 93

Experiment 3, comparison of differences in serum T4 values (mcg/100ml) between pairs of blood samples taken on seven occasions during two days, from a group of normal dogs

Comparison sample nos.	No. of pairs	Mean differences	't'
1 and 6	6	0.059	0.141
2 and 6	6	0.317	0.590
3 and 6	6	0.125	0.554
4 and 6	6	0.100	0.248
5 and 6	6	0.400	0.805
1 and 7	7	0.621	1.143
2 and 7	7	0.379	0.647
3 and 7	7	0.643	1.163
4 and 7	7	0.664	1.243
5 and 7	7	0.364	0.618

Table 94

Experiment 4, serum T4 values (mcg/100ml) in normal dogs at intervals before and after feeding. Dogs were fed at 2pm daily

Dog No.	Sample No.	1	2	3	4	5	6	7	8
	Time	5 hrs 9am	3 hrs 11am	Imm. 2.15	3 hrs 5pm	5 hrs 9am	2 hrs 11am	Imm 2.15	2 hrs 4pm
N2		1.40	1.20	0.85	1.60	1.60	1.00	1.60	1.10
N3		2.20	2.40	3.40	3.90	2.00	1.00	1.00	2.80
N17		0.60	1.00	0.60	2.20	1.80	1.00	1.20	2.60
N25		1.60	2.00	na	na	2.00	1.95	2.55	2.10
N		4	4	3	3	4	4	4	4
Mean		1.45	1.65	1.62	2.57	1.85	1.24	1.59	2.15
Standard dev.		0.66	0.66	1.55	1.19	0.19	0.48	0.69	0.76
Standard error		0.33	0.33	0.90	0.69	0.10	0.24	0.34	0.38

Table 95

Experiment 4, comparison of differences in serum T4 values (mcg/100ml) between pairs of blood samples taken at intervals before and after feeding from a group of normal dogs

Comparison sample nos.	No. of pairs	Mean differences	't'
1 and 3	3	0.217	0.419
2 and 3	3	0.083	0.182
3 and 4	3	0.950	2.854
5 and 7	4	0.263	0.772
6 and 7	4	0.350	2.333
7 and 8	4	0.563	0.930

Table 96

Experiment 5, serum T4 values (mcg/100ml) in normal dogs, immediately before and at intervals after feeding. Dogs fed at 9 a.m. on Day 1.

Dog No.	Sample no.	1	2	3	4	5	6
	Time	Imm. 8.45	2 hrs 11am	4 hrs 1pm	6 hrs 3pm	8 hrs 5pm	24 hrs 9am
N1		1.05	1.05	na	1.30	1.60	1.30
N15		2.00	1.10	2.60	2.50	1.20	2.10
N17		0.60	1.00	0.60	1.00	0.95	1.40
N23		2.00	5.20	5.20	3.20	3.00	1.90
N		4	4	3	4	4	4
Mean		1.41	2.09	2.80	2.00	1.69	1.68
Standard dev.		0.70	2.08	2.31	1.03	0.92	0.39
Standard error		0.35	1.04	1.33	0.52	0.46	0.19

na not available

Table 97

Experiment 5, comparison of differences in serum T4 values (mcg/100ml) between pairs of blood samples from normal dogs, taken at intervals before and after feeding

Comparison sample nos.	No. of pairs	Mean differences	't'
1 and 2	4	0.675	0.763
1 and 3	3	1.267	1.290
1 and 4	4	0.588	2.791
1 and 5	4	0.275	0.718
1 and 6	4	0.263	1.360

Group HS, Dogs with Suspected Hypothyroidism

The results of the T4RIA on the first blood samples taken are given in Tables 98 and 99 for the previously untreated and previously treated dogs respectively. Results are not available for HS40, in the HSU group. In the HSU group the range was 0.2 - 6.5 mcg/100ml, 2.61 ± 1.52 (mean ± SD). In the HST group the range was 0.5 - 3.2 mcg/100ml, 1.78 ± 0.98 mcg/100ml (mean ± SD).

The results of T4RIA on all samples are given in Table 100 which also shows the mean ± SD for T4 in cases where more than one sample was assayed.

Group OH, Dogs with Other Endocrine Disorders

The results of T4RIA on the dogs of this group are presented in Table 101, together with the mean and standard deviation in cases which had more than 1 blood sample assayed. The mean for the group is 2.08 ± 1.42 mcg/100ml (SD).

Group P, Dogs with Pyoderma

The results of T4RIA are recorded in Table 102 which also shows the mean and standard deviation in cases where more than one sample was assayed. The mean and standard deviation for the group were 1.75 ± 1.03 mcg/100ml, for the first samples.

Group A, Dogs with Allergic Conditions

The results of T4RIA on 45 dogs are presented in Table

Table 98

Serum T4 and T3 values at the time of first clinical examination of untreated dogs with suspected hypothyroidism (HSU)

Dog No.	Thyroxine (mcg/100ml)	Triiodothyronine (ng/ml)
HS1	0.55	0.80
HS2	0.20	na
HS3	1.60	0.95
HS4	4.90	1.80
HS5	3.90	1.70
HS6	3.10	0.70
HS7	2.80	na
HS8	3.40	1.70
HS9	3.00	4.90
HS11	1.10	0.80
HS14	2.20	1.25
HS16	0.70	1.95
HS18	3.30	1.25
HS20	0.90	0.50
HS21	3.20	0.95
HS22	2.30	1.85
HS23	2.60	1.20
HS24	1.40	0.80
HS25	4.00	0.20
HS26	1.10	na
HS27	0.50	0.25
HS28	2.80	1.60
HS29	2.40	2.20
HS30	4.20	1.70
HS32	1.25	1.25
HS33	2.20	1.60
HS34	2.20	1.40
HS36	6.40	2.00
HS38	3.20	na
HS39	1.60	1.10
HS40	na	na
HS41	6.50	1.80
HS43	3.20	1.30
HS44	2.50	1.65
HS45	3.80	2.00

na not available

n	34	30
mean	2.61	1.49
SD	1.52	0.81

Table 99

Serum T4 and T3 values at the time of first clinical examination of previously treated dogs with suspected hypothyroidism (HST)

Dog No.	Thyroxine (mcg/100ml)	Triiodothyronine (ng/ml)
HS10	3.10	1.75
HS12	0.80	0.55
HS13	0.50	0.40
HS15	2.70	1.05
HS17	1.80	1.30
HS19	1.30	0.72
HS31	0.60	0.60
HS35	1.70	0.72
HS37	2.40	1.90
HS42	3.20	2.00
HS46	0.80	0.40
HS47	2.50	1.10
N	12	12
Mean	1.78	1.04
Standard deviation	0.98	0.58

Table 100

Group HS, serum T3 and T4 values in dogs with suspected hypothyroidism

Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)
HS1	24. 8.78	0.80	0.55
HS2	2.11.76*		0.20
	2.11.76*		0.20
	15.11.76	0.50	0.60
	13.12.76	1.30	1.20
	10. 1.77	0.50	0.90
	24. 1.77	0.80	0.40
	7. 2.77	1.10	0.60
	14. 2.77	1.50	0.40
	21. 3.77	0.95	1.15
	4. 4.77	0.72	1.50
	16. 5.77	1.40	1.50
	12. 7.77	0.95	1.00
	26. 7.77	1.10	0.40
	16. 8.77	1.15	0.50
	6. 9.77	0.75	1.25
	6.10.77	0.07	0.50
	13.10.77	0.75	0.90
	22.11.77	1.75	2.10
	22.12.78	1.45	1.80
	24. 1.78	0.55	0.60
	7. 2.78	0.50	0.95
	18. 4.78	0.07	1.80
	31. 5.78	1.25	2.00
	20. 6.78	1.45	1.80
	18. 7.78	0.80	1.00
HS3	6. 6.78	0.95	1.60
	23. 6.78	1.25	0.40
	6. 7.78	1.70	0.60
	18. 7.78	2.00	0.80
	31. 8.78*		0.50
	31. 8.78*		0.50
	23. 9.78	1.48	0.60
HS4	14.11.77	1.80	4.90
	16.11.77	1.25	3.00
	7.12.77	1.70	3.00
	28. 2.78*	1.75	4.10
	28. 2.78*		4.00
	18. 4.78*	2.55	1.20
	18. 4.78*		1.90
	27. 6.78	1.70	1.20
	8. 8.78	0.80	0.70
HS5	29. 6.78	1.70	3.90
	20. 7.78	1.60	2.90
	15. 8.78	2.00	1.05
	28. 9.78	1.70	1.80
	20.11.78	2.60	2.80
	26. 3.79	1.40	2.60
	28. 5.79	0.95	3.60
HS6	24. 6.77*	0.70	3.10
	24. 6.77*	0.20	2.40
	1. 7.77	0.80	2.20
	2. 8.77*	1.10	2.70
	2. 8.77*	0.25	3.05
	15. 8.77		0.90
	15. 9.77	0.60	
	15.11.77	1.00	3.00
	16. 1.78	1.20	5.10
	15. 3.78	1.70	4.70
	21. 4.78	1.00	
	21. 7.78	0.90	3.20
	7. 8.78	1.00	8.60
	6.11.78	1.10	1.80
	18. 1.79	2.40	2.30
	12. 6.79		1.40
HS7	9. 3.78*		2.80
	9. 3.78*		2.60
	15. 3.78		4.40
	22. 3.78*		1.60
	22. 3.78*		1.80
	17. 5.78	3.80	5.90
	17. 5.78	3.00	7.60
	15. 6.78	1.50	2.80
	14. 7.78	2.30	2.60
	14. 8.78	1.80	4.30
	28. 9.78	2.30	4.60
	31.10.78	1.15	1.40
	29.11.78	2.00	4.80
	12. 1.79	1.90	5.00
	28. 2.79	3.20	5.00
	28. 3.79*		4.60
	28. 3.79*	1.20	4.50
	15. 6.79		2.60

* duplicate results

Table 100 (contd.)

Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)	Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)
HS8	5. 2.77	1.70	3.40	HS10	30. 5.77	1.65	2.90
	14. 2.77	2.00	4.10	(cont)	21. 7.77*	1.30	3.00
	19. 2.77	1.70	3.60		21. 7.77*		3.70
	14. 3.77	1.45	3.80		24. 9.77*		5.60
	22. 4.77	1.00	4.90		24. 9.77*	1.85	5.50
	3. 6.77	1.70	1.60		8.10.77*	1.70	3.90
	18. 7.77	1.20	6.50		8.10.77*		4.00
	19. 8.77	0.52	1.40		22.10.77*	1.75	6.20
	17.10.77	1.00	1.90		22.10.77*		5.00
	17.11.77	1.20	2.90		11.11.77	1.75	7.20*
	16. 2.78		1.80		11.11.77		7.40*
	24. 4.78	1.70	3.10		21. 1.78	1.00	3.00
	26. 6.78	0.70	3.80		18. 3.78	1.70	3.00*
	30. 6.78	0.75	1.70		18. 3.78		3.90*
	23.10.78	1.40	2.50		15. 7.78	1.75	4.60*
	23.11.78	0.85	2.70		15. 7.78		4.20*
	5. 3.79	1.50	3.40		16. 8.78	0.72	1.90*
					16. 8.78		1.90*
HS9	22. 8.77	4.90	3.00		25.10.78	1.85	5.80*
	25. 8.77	1.40	1.30		25.10.78		4.80*
	8. 9.77	2.10	2.40		13.12.78	0.75	1.90
	22. 9.77	1.65	2.10		27. 1.79	0.55	1.30
	6.10.77	1.60	3.00				
	13.10.77	1.10	1.60	HS11	13.12.76	0.80	1.10
	20.10.77	1.20	1.40		17. 2.77	0.54	1.80
	3.11.77		8.10		2. 3.77	0.72	1.00
	24.11.77	1.30	1.50		2. 3.77	0.50	0.45
	9. 2.78	4.50	2.40		17. 3.77	0.35	1.70
	23. 2.78	1.75	1.00		29. 3.77	0.65	1.25
	23. 3.78	1.50	2.10		12. 4.77	0.70	2.60
	24. 4.78*		0.80		10. 5.77	0.25	0.50
	24. 4.78*		0.70		26. 5.77	0.50	0.90
	28. 4.78*	0.40	0.90		28. 7.77	0.40	1.25
	28. 4.78*	0.75	1.60		1.12.77	1.75	1.25
	1. 6.78	1.25	1.50		13. 2.78	1.30	3.90
	29. 6.78	1.60	2.40		27. 2.78	1.40	1.25
	18. 8.78	1.10	1.10				
	7. 3.79	1.25	1.30	HS12	10. 7.78	0.55	0.80
					1. 2.79	1.00	2.10
HS10	10. 2.77*	1.75	3.10	HS13	31. 3.77	0.40	0.50
	10. 2.77*		3.10		14. 4.77	0.72	1.00
	17. 2.77		1.80		14. 4.77		2.70
	24. 2.77	1.30	3.70		5. 5.77	1.00	1.80
	9. 3.77*	0.72	2.90		3. 6.77		0.65
	9. 3.77*		3.10		4. 7.77	0.60	0.20
	28. 3.77	1.10	3.00		4. 8.77	0.72	1.20
	7. 5.77	0.72	2.10		5. 9.77	0.65	1.40

* duplicate results

Table 100 (contd.)

Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)	Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)
HS13	5. 9.77		2.40	HS21	30.12.76	0.95	3.20
(cont)	10.11.77	1.10	2.20		20. 1.77	0.95	3.10
	10.11.77		3.30				
	20. 3.78	1.10	3.60	HS22	8.12.76	1.85	7.00
	20. 3.78		3.60		8.12.76		2.30
	24. 6.78	1.25	3.90		4. 2.77	1.25	1.50
	24. 6.78		4.00		11. 2.77	1.60	3.90
	16.10.78	1.60	1.10		3. 3.77	0.65	1.00
	27.10.78	1.70	3.20		1. 4.77	0.70	1.40
	27.10.78		3.60		4. 5.77	0.65	1.00
	5. 3.79	0.65	0.80		19. 8.77	1.00	1.80
	5. 3.79		1.35		4.11.77	0.65	6.30
	9. 7.79		0.85		4.11.77		1.80
HS14	4. 4.78	1.25	2.20	HS23	29.11.76	1.20	2.60
	4. 5.78	1.00	0.75		17. 1.77	1.60	0.80
	20. 2.79	2.30	1.00		27. 1.77	1.50	0.70
	20. 3.79	2.25	1.00		3. 3.77	0.70	2.30
	8. 5.79	2.40	1.70		17. 3.77	1.60	0.50
	3. 7.79		0.80		21. 4.77	1.00	0.50
					3. 6.77	1.40	1.40
HS15	18. 7.78	1.05	2.70		26. 9.77	2.20	2.50
HS16	11. 5.78	1.95	0.70	HS24	4.11.76	0.80	1.40
	25. 5.78	1.95	0.80		22.11.76	0.20	
					6. 2.76	2.10	3.20
HS17	29. 6.78	1.30	1.80		20.12.76	1.65	2.00
					11. 1.77	1.80	2.60
HS18	18. 1.77	1.25	3.30		17. 2.77		3.70
	28. 1.77	1.45	2.50		24. 2.77	2.20	2.10*
	15.11.77	1.15	1.40				
	30. 6.78		0.20				
	28. 9.78	1.10	1.20	HS25	2.12.76	2.00	4.00
					10. 1.77	3.15	1.40
HS19	2. 6.77	0.72	1.30		25. 2.77	1.00	3.60
	26. 8.77	0.80	4.00		25. 4.77	0.95	4.20
	19.12.77	1.00	2.00				
	7. 1.78	1.40	1.25	HS26	1. 3.77		1.10
	3. 2.78	0.45	3.00		14. 3.77	0.10	1.50 *
	3. 3.78	0.72	2.20		28. 3.77	1.10	1.30 *
	25. 4.78	1.60	2.40				
	9. 6.78	1.25	1.40				
	16. 1.79	0.60	1.30	HS27	21. 7.77	0.25	0.50
					22. 7.77	0.60	0.60
HS20	30. 3.78	0.50	0.90		2. 8.77	0.50	1.90*
	27. 4.78	1.15	1.20				
	25. 5.78	1.10	1.00		16. 8.77	1.05	4.00
					29.10.77	0.20	0.70
					23. 3.78	0.45	4.30

* duplicate results

Table 100 (contd.)

Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)	Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)
HS28	11. 3.77	1.60	2.80	HS38	4.12.78		3.20
	5. 4.77	0.80	1.10		4.12.78		2.40
					10. 1.79	0.46	1.20
HS29	2. 3.77	2.20	2.40		30. 1.79	1.70	0.90
	21. 3.77	0.70	0.80		27. 2.79		0.90
	9. 6.77	0.03			27. 2.79		0.80
	8.11.77	1.50	3.70		3. 4.79	3.25	2.40
					3. 4.79	1.55	0.60
HS30	28. 2.77	1.70	4.20		3. 4.79		.80
	15. 3.77	1.90	5.00		5. 6.79	2.00	1.00
	4. 4.77	1.50	4.80				
	12. 4.77		1.80	HS39	15. 2.79	1.10	1.60
	26. 4.77	1.15	2.10		17. 2.79	1.70	2.20
	16. 6.77	0.55	2.00		17. 2.79	1.15	0.60
	24.10.77	1.30	5.40		17. 2.79		1.25
					5. 3.79	2.10	3.40
HS31	4.10.77	0.60	0.60		19. 3.79	1.90	6.10
	6.11.78	1.40	2.70		30. 3.79	4.00	7.00
					30. 3.79	1.10	2.20
HS32	19. 9.78	1.25	1.25		23. 4.79	1.10	4.10
	27. 9.78	1.20	1.40		7. 5.79	1.95	4.00
HS33	10.11.76	1.60	2.20				
	5. 1.77	0.25	1.20	HS41	6. 3.79	1.80	6.50
	24. 1.77	0.72	2.00		19. 3.79	2.40	4.10
	5. 2.77	1.45	2.00		30. 3.79	2.85	4.20
	5. 3.77		1.40		23. 4.79	1.65	3.00
	28. 5.77*	1.75	5.25		7. 5.79	1.60	4.60
	28. 5.77*		5.40				
	5.11.77	2.40	5.10	HS42	19. 4.79	2.00	3.20
	23.11.77	0.45	1.00				
	3. 3.78	1.20	2.40				
	5. 6.78	0.50	0.80	HS43	5. 6.79	1.30	3.20
HS34	7.11.77	1.40	2.20	HS44	28. 5.79	1.65	2.50
	11.11.77	0.95	2.90		30. 5.79	1.30	1.90
		1.00	3.20		6. 6.79	1.05	1.60
HS35	1. 4.77	0.72	1.70	HS45	24. 5.79	2.00	3.80
	20. 5.77	0.10	2.50				
				HS46	27. 4.79	0.40	0.80
HS36	11. 9.78	2.00	6.40		1. 5.79	1.60	3.00
	19. 9.78	1.20	6.00				
	10.10.78	1.70	5.20	HS47	15. 5.79	1.10	2.50
HS37	27.11.78	1.90	2.40				

* duplicate results

Table 100 (contd.)

Group HS, Serum T3 (ng/ml) and T4 (mcg/100ml) mean and standard deviation of values

Dog No.	T3		T4	
	Mean	SD	Mean	SD
HS2	0.93	0.45	1.01	0.58
HS3	1.48	0.40	0.71	0.41
HS4	1.65	0.54	2.66	1.50
HS5	1.70	0.51	2.66	0.98
HS6	1.00	0.55	3.17	1.92
HS7	2.20	0.84	3.83	1.64
HS8	1.27	0.44	3.12	1.32
HS9	1.73	1.18	2.11	1.60
HS10	1.33	0.47	3.80	1.61
HS11	0.76	0.45	1.46	0.92
HS12	0.77	0.32	1.45	0.92
HS13	0.96	0.41	2.06	1.27
HS14	2.20	1.26	1.24	0.58
HS16	1.95	0.00	0.75	0.07
HS18	1.24	0.15	1.72	1.20
HS19	0.95	0.39	2.09	0.94
HS20	0.92	0.36	1.03	0.15
HS21	0.95	0.00	3.15	0.07
HS22	1.04	0.48	2.80	0.08
HS23	1.40	0.45	1.41	0.92
HS24	1.46	0.79	2.50	0.84
HS25	1.78	1.03	3.30	1.29
HS26	0.60	0.70	1.55	0.73
HS27	0.50	0.30	2.00	1.74
HS28	1.20	0.56	1.95	1.20
HS29	1.11	0.94	2.30	1.45
HS30	1.35	0.47	3.61	1.58
HS31	1.00	0.56	1.65	1.48
HS32	1.22	0.03	1.32	0.11
HS33	1.15	0.72	2.61	1.76
HS34	1.12	0.25	2.76	0.51
HS35	0.41	0.44	2.10	0.56
HS36	1.63	0.40	5.86	0.61
HS38	1.79	1.00	1.42	0.90
HS39	1.79	0.92	3.24	2.09
HS41	2.06	0.54	4.48	1.27
HS44	1.33	0.30	2.00	0.45
HS46	1.00	0.85	1.90	1.55

Table 101

Group OH, serum T3 and T4 values in dogs with other hormonal disorders

Dog No.	Date of sample	T3 (ng/ml)	T4 (mcg/100ml)
OH1		0.75	0.85
OH2		1.60	1.60
OH3	2. 5.78	1.60	2.60
	18. 5.78		0.60
	4. 7.78	1.70	3.10
OH4		1.05	2.80
OH5		1.05	2.50
OH6	2. 6.78	1.00	0.70
	5. 6.78	1.00	1.40
OH7		1.10	1.00
OH8	13. 7.77	1.60	3.00
	15. 9.77	1.50	2.40
OH9		2.05	7.60
OH10	11. 7.77	1.10	
	26. 7.77	0.95	
	25. 8.77	1.50	1.20
	23. 9.77	0.95	
	31. 5.78	1.85	1.70
OH11		0.25	0.85
OH12	14. 2.78	1.35	
	16. 3.78		0.95
	20. 6.78	1.10	0.60
OH13	22. 8.78	1.00	0.65
	20. 9.78	0.75	1.00
OH14	14. 9.78	0.80	1.10
	13.10.78	1.30	1.10
OH15		0.85	1.20
OH16	10.12.76	1.50	
	28.12.76	2.05	
	24. 3.77	2.75	3.10
	26. 6.77	0.80	1.60
OH17	22. 3.77	0.60	1.40
	26. 9.77	0.80	1.40
	2. 3.78	1.60	3.00
	1. 5.78	1.20	2.00
	2. 6.78	0.30	0.40
	20. 6.78	1.25	2.60
OH18	3.10.77	1.45	
	7.10.77	1.15	1.40
	17.10.77	1.50	4.20
	7.11.77	1.60	4.10
OH19		1.60	2.40
OH20	16. 5.78	1.00	0.60
	7. 7.78	1.45	1.40
OH21		0.50	2.50
OH22		1.45	4.60
OH23	13. 7.78	1.05	1.08
	15. 8.78	1.15	0.40
	5. 9.78		0.90
OH24	13. 6.77	1.65	
	7. 7.77	1.40	1.40
	18. 7.77	1.50	1.80
OH25		0.85	2.30
OH26	14. 2.77	1.65	5.10
	31. 5.77	2.25	2.00
OH27	26. 1.77	0.72	2.20
	13. 7.77	4.15	
	26. 7.77	1.05	3.80
OH28	15. 8.77*	0.72	0.70
	15. 8.77*		1.70
	4. 5.79*	0.60	
	4. 5.79*	1.00	0.40
	4. 5.79*		1.40
	19. 5.78	0.72	0.70
	31. 5.78	0.35	0.50

* duplicate results

Table 101 (contd.)

Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)
OH29		1.75	1.55
OH30		1.20	1.90
OH31		0.75	1.80
OH32	25. 3.77	1.55	
	16. 8.77	1.20	3.20
	27. 3.78	1.65	5.40
	2. 4.79	1.45	3.20
OH34		0.75	2.00
OH35		1.70	1.40
OH36	10. 4.78	1.60	2.80
	18. 6.78	1.60	2.80
OH37	5. 3.77	1.95	3.20
	23. 3.77*	1.30	6.20
	23. 3.77*		6.60
	28. 4.77*	1.80	7.50
	28. 4.77*		5.80
OH38	7. 3.79	2.60	3.30
	15. 3.79	0.25	0.80
OH39	6. 3.79	0.72	1.10
	13. 3.79	1.05	1.40
OH40	2. 3.79	1.05	2.00
	7. 3.79	0.80	1.40
OH41		0.35	1.30
OH42		0.60	0.80
OH43		2.10	4.40
OH44		1.35	2.50
OH45	20. 4.79	1.40	2.10
	25. 4.79	2.15	2.90
OH46	24. 5.79	0.50	0.60
	3. 7.79		1.30
OH47	10. 8.78	1.05	0.60
	21. 8.78	0.75	0.60

* duplicate results

Table 101 (contd.)

Group OH, serum T3 (ng/100ml) and T4 (mcg/100ml) mean and standard deviation of values

Dog No	T3 Mean	T3 SD	T4 Mean	T4 SD
OH3	1.65	0.07	2.10	1.32
OH6	1.00	0.00	1.05	0.49
OH8	1.55	0.07	2.70	0.43
OH10	1.27	0.39	1.45	0.35
OH12	1.22	0.17	0.77	0.24
OH13	0.87	0.17	6.82	0.24
OH14	1.05	0.35	1.10	0.00
OH16	1.77	0.82	2.35	1.06
OH17	0.96	0.47	1.80	0.94
OH18	1.42	0.19	3.23	1.59
OH20	1.22	0.32	1.00	0.56
OH23	1.10	0.07	1.03	0.71
OH24	1.52	0.12	1.60	0.28
OH26	1.95	0.42	3.50	1.50
OH27	1.97	1.89	3.00	0.80
OH28	0.68	0.23	0.90	0.52
OH32	1.46	0.19	3.93	1.03
OH36	1.60	0.00	2.80	0.00
OH37	1.68	0.34	5.86	1.61
OH38	1.42	1.66	2.05	1.76
OH39	0.88	0.23	1.25	0.21
OH40	0.92	0.17	1.70	0.42
OH45	1.77	0.53	2.50	0.56
OH46			0.95	0.49
OH47	0.9	0.21	0.60	0.00

Table 102

Group P, serum T3 and T4 values in dogs with pyoderma

Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)	Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)
P1	24. 1.77	1.00	1.50	P24	28. 6.77	0.72	0.70
	28. 2.77	1.50	3.00		21. 4.78	1.15	0.60
	14. 3.77	1.30	1.60		19. 6.78	0.85	0.90
P3		0.80	0.80	P25	25. 7.79	1.30	0.90
					15. 8.78	1.50	0.95
P4		0.72	0.70		5. 9.78	1.45	1.00
					26.10.78	1.45	1.00
P5		0.60	0.60				
				P26		0.95	1.60
P6	28.12.76	1.50	2.00				
	7. 4.77*	2.25		P27		0.50	2.20
	7. 4.77*	1.55					
				P28	25. 7.78	0.03	
P7		0.55	1.10		15. 8.78	0.90	0.75
P8		1.80	3.60	P29		0.60	1.30
P9		0.45	0.75	P31		0.75	0.50
P10		0.15	1.00	P32		0.72	2.90
P12		0.50	0.45	P33		0.72	0.45
P13		1.10	2.40	P34		1.25	2.50
P14		0.03	0.70	P35	9.12.77	1.10	1.00
					20.12.77	1.05	2.50
P15	3. 3.77	1.00	2.40				
	3. 3.77	1.05	0.60	P40		0.80	1.90
P16		2.35	3.30	P41		1.60	2.60
P19		1.05	1.00	P46		0.95	1.90
P20		1.05	3.30	P47		1.50	3.20
P21	23. 2.79	3.25		P49		1.50	1.80
	19. 5.79	0.95	2.00				
	10. 2.78	1.95		P50		1.35	1.40
	27. 2.78	1.75	4.60				
	1.11.78	2.25	4.00	P51	12.10.78	0.80	2.60
	18. 1.79	1.45	3.80		7.12.78	1.75	2.60
					22. 1.79	2.20	1.10
P22		0.72	0.60				
P23		1.80	3.00				

* duplicate results

SKIN THICKNESS

Results

The measurement of skin thickness, obtained from the 15 sites on each dog, are recorded in Tables 42, 43, 44, 45 for Groups 1, 2, 3 and 4 respectively. Tables 46 and 2 give the abbreviations used for skin sites and breed of dog, respectively. For each group, the mean and standard deviation of the measurements at each site are given in Table 47. The mean and standard deviation of the measurements at each site, for each breed, irrespective of the dog's state of health are given in Table 48.

One-way analyses of variance was performed on the data (Table 47). There was only one skin site with a statistically significant difference in thickness, in the 4 groups of dogs. This was the groin and none of the other sites showed any significant difference between the groups. In order to detect where the significance lay between the 4 groups of dogs in respect of the groin, the data were examined by Duncan's multiple range test to obtain significant subsets. The results of this are shown in Table 49 the skin thickness of the groin in Group 2 (hypothyroid dogs) differed significantly from that of the dogs in Group 1 (normal) and Group 4 (dogs with non-hormonal conditions) but did not differ significantly from that of the dogs with other hormonal conditions, Group 3. The thickness of groin skin did not differ significantly between Groups 1, 3 and 4. The f, or variance, ratio of the groin skin thickness was 2.95 and the degree of significance $P < 0.05 > 0.01$.

Having ascertained this difference between the groups, the data were re-worked by the same methods to investigate whether there were significant differences in skin

Table 102 (contd.)

Group P, serum T3 (ng/ml) and T4 (mcg/100ml) mean and standard deviation values

Dog No.	T3		T4	
	Mean	SD	Mean	SD
P1	1.26	0.25	2.03	0.84
P6	1.76	0.42		
P15	1.02	0.03	1.50	1.27
P21	1.93	0.78	3.72	
P24	0.90	0.22	0.73	0.15
P25	1.42	0.08	0.96	0.04
P28	0.46	0.61		
P35	1.07	0.03	1.75	1.06
P51	1.04	0.40	2.10	0.76
P52	2.39	2.43	1.60	0.88
P53	0.82	0.43	1.48	0.73
P56	1.65	0.21	4.45	1.06
P59	1.15	0.10	2.75	0.21
P60	0.67	0.40	1.20	0.35
P61	1.97	0.90	3.06	1.30
P65	0.53	0.26	1.17	0.53
P78	1.73	1.38	2.46	1.40
P79	1.23	0.73	2.85	1.20
P80	1.01	0.76	1.05	0.07
P82	1.65	0.63	1.70	1.13
P83	1.37	0.03	2.60	1.69
P87	1.42	0.74	1.95	0.21
P93	1.10	0.07	0.70	0.42
P94	1.47	0.03		
P98	1.23	0.73	1.70	1.13

103 which also gives the mean and standard deviation when a case was sampled more than once. The mean and standard deviations were 2.15 ± 1.37 mcg/100ml.

Group EP, Dogs with External Parasitism

The results of T4RIA are presented in Table 104. The mean and standard deviation of T4 values in blood samples taken at the first examination of 36 of the dogs were 1.84 ± 1.28 mcg/100ml.

The results of T4RIA for all groups are illustrated in Figure 10.

Table 103

Group A, serum T3 and T4 values in dogs with allergic disorders

Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)
A1	26. 4.77	1.0	0.9
	10.10.77	1.25	
A2	5. 9.77	0.05	5.00
	23. 9.77	1.00	0.50
A3		1.35	
A4		1.05	2.00
A5		1.50	2.00
A7	12. 5.78		4.50
	26. 5.78	1.50	1.90
A8	19. 5.77	1.40	2.10
	19. 8.77	1.25	0.90
A9	6. 7.77	0.90	2.10
	19.10.77	1.50	3.00
A10		5.00	
A11		1.15	3.30
A12		0.60	1.60
A13	6. 6.77	1.05	2.50
	2. 6.78	1.10	0.70
A14	1. 6.77	1.40	2.20
	8. 6.77	1.40	2.20
A15		0.75	0.60
A16	17. 6.77	1.25	6.00
	24. 6.77	2.40	5.80
A17		0.35	0.90
A18		2.35	
A19	27.10.77	0.75	0.60
	31.10.77	1.15	2.90
A20		1.05	
A21		1.05	5.10
A22	15. 8.78	1.35	0.70
	12. 9.78	1.40	0.90
A23		1.25	2.40
A24		2.10	1.90
A25	2.11.77	1.60	1.50
	27. 6.78	1.45	2.40
	30. 5.78	2.10	1.40
A26	18. 5.78	0.60	1.70
	20. 6.78	2.10	1.40
A27		0.60	0.59
A28		1.15	2.90
A29		1.15	1.50
A30	7. 9.77	0.35	0.30
	3. 3.78	1.90	1.00
	25. 5.78	0.40	
A32		1.10	0.45
A33		1.45	0.80
A34	1. 6.78	1.50	2.40
	13. 6.78	1.25	1.00
A36	1. 5.78*	1.50	1.40
	1. 5.78*	1.60	2.00
	30. 5.78	1.35	2.10
A40		0.55	1.60
A41		1.05	1.50
A42		0.75	1.10
A44		1.00	1.90

* duplicate results

Table 103 (contd.)

Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)
A45	21. 9.78	1.15	2.00
	24.10.78	0.75	0.60
	20.11.78	1.05	1.30
A46		0.45	2.20
A47		0.75	1.10
A48	16.11.78	1.40	2.60
	7.12.78	0.95	1.70
A50		1.25	3.30
A51	19. 5.78	1.10	2.20
	6. 6.78	2.10	1.80
A52		1.40	4.20
A53		1.50	5.40
A54	15.11.77	0.50	1.20
	6.12.77	2.05	3.50
A55		1.25	2.00
A56	21. 9.78	0.55	2.00
	17.11.78	1.30	0.75
A57		0.90	2.80

Table 103

Group A, serum T3 (ng/ml) and T4 (mcg/100ml) in mean and standard deviation values

Dog No.	T3		T4	
	Mean	SD	Mean	SD
A1	1.12	0.12		
A2	0.52	0.67	2.75	2.25
A7			3.20	1.30
A8	1.32	0.16	1.50	0.85
A9	1.20	0.42	2.55	0.63
A13	1.07	0.03	1.60	0.90
A14	1.40	0.00	2.20	0.00
A16	1.82	0.81	5.90	0.14
A19	0.95	0.28	1.75	1.62
A22	1.37	0.03	0.80	0.14
A25	1.72	0.32	1.43	1.00
A26	1.35	1.06	1.55	0.21
A30	0.88	0.88	0.65	0.49
A34	1.37	0.17	1.70	0.99
A36	1.48	0.12	1.83	0.38
A45	0.98	0.20	1.30	0.70
A48	1.17	0.32	2.15	0.63
A51	1.60	0.70	2.00	0.20
A54	1.27	1.09	2.35	1.62
A56	0.92	0.53	1.37	0.88

Table 104

Group EP, serum T3 and T4 values in dogs with external parasitism

Dog No.	Date of samples	T3 (ng/ml)	T4 (mcg/100ml)
EP1		0.03	0.50
EP2		1.75	4.60
EP4		1.45	1.00
EP5		1.45	4.40
EP8	10. 1.77	1.50	2.10
	21. 7.77	0.75	1.60
EP9	10. 1.77	3.00	4.90
	6. 6.78	0.75	3.00
EP10		0.72	1.00
EP11		1.80	0.50
EP12		0.72	2.70
EP13		0.90	1.40
EP15	20. 7.78	1.40	1.40
	5. 9.78	1.00	3.80
EP16		1.10	0.30
EP17			2.30
EP19			0.70
EP20		1.00	0.40
EP21		0.45	1.50
EP22		0.03	0.40
EP23	21. 7.77	1.40	2.00
	10. 1.77	2.75	
EP24		0.95	2.20
EP27		0.80	0.90
EP30	18. 1.78	0.72	0.70
	15. 6.78	2.10	4.40
EP31		1.35	2.90
EP34		1.15	0.90
EP35		0.50	2.20
EP36	9. 8.77	1.70	
	19. 8.77	1.65	6.85
	22. 3.78	1.50	4.60
EP37		0.72	0.40
EP38		1.30	2.10
EP39		0.80	3.00
EP40	8. 6.78	1.45	1.10
	7. 9.78	0.85	2.30
EP41		1.10	3.40
EP42		1.25	
EP43		0.85	1.50
EP44		0.95	0.40
EP45	22. 2.79	1.75	2.20
	15. 3.79	0.40	0.30
EP46	12. 3.79	1.75	3.00
	16. 4.79*	1.80	2.60
	16. 4.79*	1.78	2.80
EP47	19.12.78	0.95	2.20
	5. 4.79	1.15	0.80
EP48		1.50	1.20
EP49		1.60	4.00

* duplicate results

Table 104

Group EP, serum T3 (ng/ml) and T4 (mcg/100ml) mean and standard deviation values

Dog No.	T3		T4	
	Mean	SD	Mean	SD
EP8	1.12	0.53	1.85	0.35
EP9	1.87	1.12	3.95	0.95
EP15	1.20	0.20	2.60	1.20
EP23	2.07	0.95		
EP30	1.41	0.97	2.55	1.85
EP36	1.67	0.03	5.73	1.13
EP40	1.15	0.42	1.70	0.84
EP45	0.99	0.95	1.25	1.34
EP46	1.78	0.02	2.80	0.20
EP47	1.05	0.14	1.50	0.99

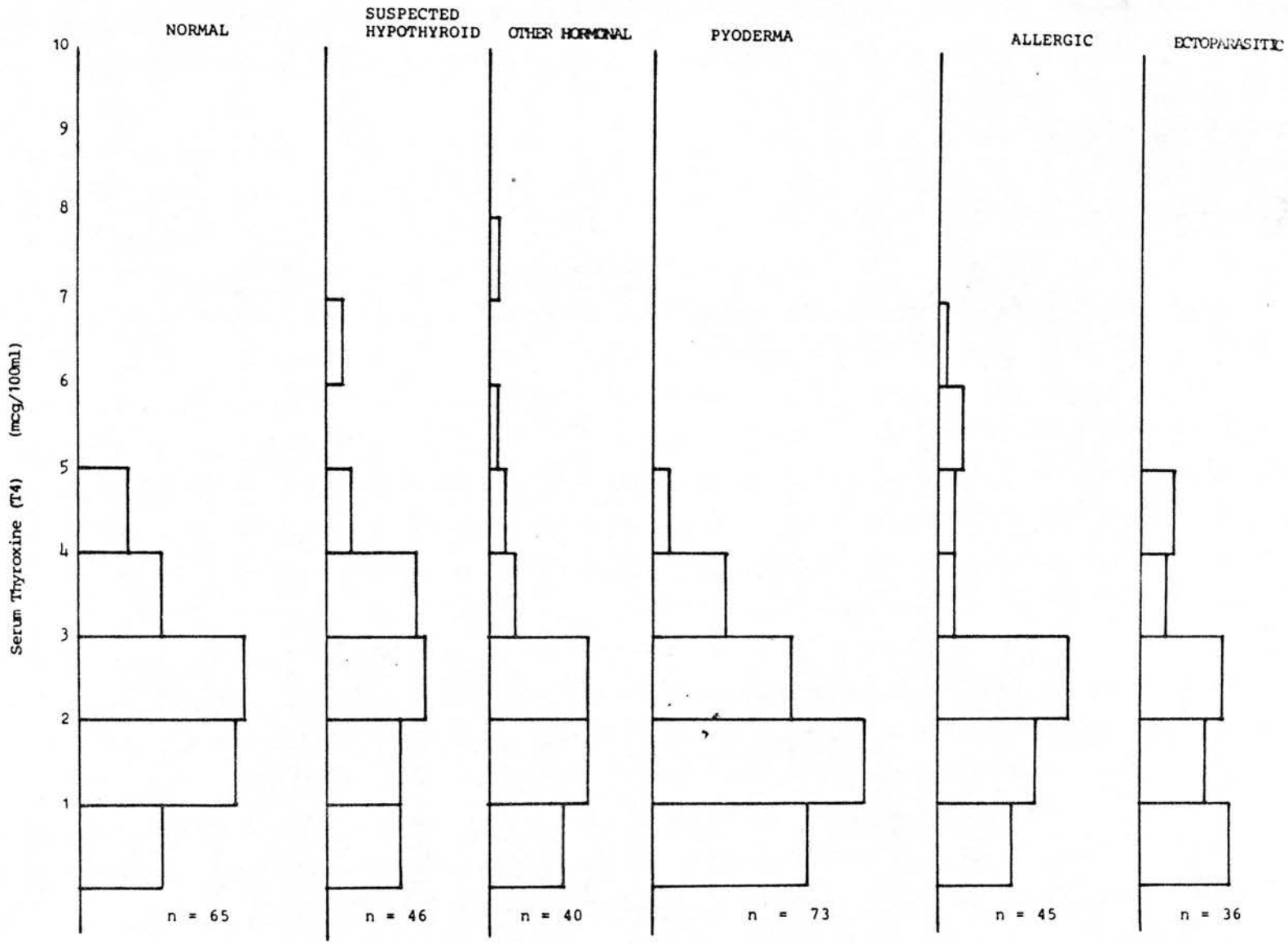


Figure 10 Comparative distribution of serum thyroxine in different dogs at time of first examination

SERUM TRIIODOTHYRONINE VALUES

Group N, Normal Dogs

The results of the T3RIA of blood samples taken at the time of the first clinical examination are presented in Table 88, for 63 of the 68 dogs in Group N. The range of first values was 0.40 - 3.70 ng/ml, with mean and standard deviation of 1.58 ± 0.76 ng/ml i.e. in SI units 0.62 - 5.70 nmol/l, and 2.43 ± 1.17 nmol/l (m± SD).

Both for dogs for which only a single T3 value is available and for those which were serially sampled, the results are presented in Table 89 . The mean and standard deviation for dogs which were sampled more than once are also included in the Table. As different numbers of T3RIA were conducted on different dogs, the results are given here as the range of the means, i.e. 0.50 - 3.50 ng/ml. In SI units, this is 0.77 - 5.39 nmol/l.

The results of the 5 experiments were as follows.

Experiment 1

The results of T3RIA on blood samples obtained from a group of 9 normal dogs, 2 hours before and 2 hours after feeding, are presented in Table 105. No significant differences were found when the 't' test was applied.

Experiment 2

Table 106 presents the results of T3RIA on serum obtained from dogs immediately after and 2 and 19 hours

Table 105

Experiment 1, serum T3 values (ng/ml) in normal dogs, 2 hours before and 2 hours after feeding

Dog No.	2 hours before feeding	2 hours after feeding
N10	3.70	2.50
N11	0.95	0.90
N12	1.50	1.05
N13	1.00	2.00
N14	1.80	1.75
N15	1.75	1.75
N23	1.00	1.55
N32	1.10	1.65
N34	0.72	1.15
No 9		
Mean	1.50	1.59
Standard deviation	0.91	0.50
Standard error	0.30	0.67

No. of pairs 9

Mean difference 8.667

't' 0.401

Table 106

Experiment 2, serum T3 values (ng/ml) in normal dogs at intervals after feeding

Dog No.	Immediately after	2 hours after	19 hours after
N4	1.65	2.00	2.65
N17	1.25	1.20	1.20
N23	1.35	1.20	0.80
N36	1.00	0.95	1.30
N68	0.40	0.50	0.65
No.	5	5	5
Mean	1.13	1.17	1.32
Standard dev.	0.47	0.54	0.79
Standard error	0.21	0.24	0.35

Comparison	No. of pairs	Mean difference	't'
Immediately after and 2 hours after	5	0.04	0.459
Immediately after and 19 hours after	5	0.19	0.752

after feeding. The paired 't' test when applied revealed no significant differences in the T3 values at the different times.

Experiment 3

The T3RIA values obtained in Experiment 3 are set out in Table 107, for samples assayed on 7 occasions during 2 days. Application of the 't' test to the data arranged in pairs revealed no significant differences (Table 108).

Experiment 4

The results of T3RIA are shown in Table 109. The 't' test revealed no significant differences (Table 110).

Experiment 5

The results of T3RIA are given in Table 111. No significant differences were found between the T3 values at the different intervals when the 't' test was conducted in pairs of sets of assays (Table 112), except in the case of pairs 1 and 3, i.e. the groups of samples taken immediately after and 4 hours after feeding. No reason for this single occurrence in 24 comparisons in 5 experiments could be ascribed.

Group HS, Dogs with Suspected Hypothyroidism

The results of T3RIA on the blood samples taken at the time of the first clinical examination are given in Tables

Table 107

Experiment 3, serum T3 values (ng/ml) in normal dogs on seven occasions during two days

		Day 1					Day 2	
Dog No.	Sample No. / Time	1 9 am	2 noon	3 2.15pm	4 5pm	5 9am	6 noon	7 4pm
N5		1.10	1.10	1.30	1.00	1.60	1.45	1.00
N6		1.15	0.80	0.90	0.65	0.75	1.20	1.20
N15		1.15	1.00	1.45	1.35	1.35	1.35	1.40
N16		1.20	1.75	1.50	1.50	1.50	1.20	1.20
N17		0.95	0.95	0.95	1.20	1.00	1.50	1.20
N23		1.20	1.20	1.15	1.15	1.15	1.55	na
N24		1.20	1.85	1.65	1.10	0.72	na	1.20
N		7	7	7	7	7	6	6
Mean		1.33	1.24	1.27	1.14	1.15	1.37	1.20
Standard dev.		0.09	0.41	0.28	0.27	0.35	0.15	0.13
Standard error		0.03	0.15	0.11	0.10	0.13	0.06	0.05

Table 108

Experiment 3, Comparison of differences in T3 values (ng/ml) between pairs of blood samples taken on seven occasions during two days, from a group of normal dogs

Comparison sample no.	No. of pairs	Mean differences	't'
1 and 6	6	0.25	2.953
2 and 6	6	0.24	1.497
3 and 6	6	0.16	1.280
4 and 6	6	0.23	1.775
5 and 6	6	0.15	1.070
1 and 7	6	0.07	1.419
2 and 7	6	0.04	0.217
3 and 7	6	0.09	0.719
4 and 7	6	0.07	0.594
5 and 7	6	0.04	0.268

Table 109

Experiment 4, serum T3 values (ng/ml) in normal dogs at intervals before and after feeding. Dogs were fed at 2 p.m. daily

		Day 1				Day 2			
Dog No.	Sample No.	1	2	3	4	5	6	7	8
	Time	5 hrs before 9am	3 hrs before 11am	Imm. after 2.15	3 hrs after 5pm	5 hrs before 9am	2 hrs before 11am	Imm. after 2.15	2 hrs after 4pm
N2		0.90	2.30	0.80	0.90	0.72	0.85	1.05	0.90
N3		1.00	2.30	1.25	1.15	1.05	0.85	1.05	1.25
N17		1.25	1.55	1.45	1.10	1.65	1.05	1.85	1.60
N25		1.40	1.90	1.40	na	na	na	na	na
N		4	4	4	3	3	3	3	3
Mean		1.14	2.01	1.23	1.05	1.14	0.91	1.32	1.25
St. dev.		0.23	0.36	0.29	0.13	0.47	0.12	0.46	0.35
St. error		0.11	0.18	0.15	0.08	0.27	0.07	0.27	0.20

na: not available

Table 110

Experiment 4, Comparison of differences in serum T3 values (ng/ml) between pairs of blood samples taken at intervals before and after feeding for a group of normal dogs

Comparison sample nos.	No. of pairs	Mean differences	't'
1 and 3	4	0.09	1.059
2 and 3	4	0.79	2.564
3 and 4	3	0.12	0.896
5 and 7	3	0.18	1.841
6 and 7	3	0.40	2.000
7 and 8	3	0.07	0.489

Table 111

Experiment 5, serum T3 values (ng/ml) in normal dogs, immediately before and at intervals after feeding. Dogs fed at 9 a.m. on Day 1

		Day 1					Day 2
Dog No.	Sample No.	1	2	3	4	5	6
	Time	Imm. before 8.45am	2 hrs after 11am	4 hrs after 1pm	6 hrs after 3pm	8 hrs after 5pm	24 hrs after 9am
N1		0.90	0.65	1.45	0.55	0.65	0.65
N15		1.20	1.25	1.55	1.15	1.75	1.20
N17		0.72	1.20	1.50	1.20	1.00	1.20
N20		0.50	0.65	0.90	0.65	0.85	0.50
N23		1.10	2.05	1.85	2.00	1.75	1.65
N		5	5	5	5	5	5
Mean		0.88	1.16	1.45	1.11	1.20	1.04
St. Dev.		0.28	0.57	0.34	0.58	0.52	0.47
St. error		0.13	0.26	0.15	0.26	0.23	0.21

Table 112

Experiment 5, Comparison of differences in serum T3 values (ng/ml) between pairs of blood samples for normal dogs, taken at intervals before and after feeding

Comparison sample nos.	No. of pairs	Mean differences	't'	
1 and 2	5	0.28	1.343	
1 and 3	5	0.57	6.448	**
1 and 4	5	0.23	1.047	
1 and 5	5	0.32	2.021	
1 and 6	5	0.16	1.014	

** $P < 0.01$

98 and 99 for the previously untreated and previously treated dogs respectively. In the HSU group the range was 0.2 - 4.9 ng/ml, 1.49 ± 0.81 mean and standard deviation. In the HST group, the range was 0.40 - 2.00 ng/ml, 1.04 ± 0.58 mean and standard deviation.

A number of dogs were sampled more frequently than once and the results of T3RIA for all samples assayed are given in Table 100. The mean and standard deviation are given for each dog which had more than 1 sample assayed.

Groups OH, P, A and EP

The results of T3 assay on the dogs of these groups are recorded in the following Tables

Group	Table
Dogs with Other Hormonal Conditions (OH)	101
Dogs with Pyoderma (P)	102
Dogs with Allergic Disorders (A)	103
Dogs with External Parasitism (EP)	104

When more than one sample from a dog was assayed for T3, the mean and standard deviation of results is given.

At the time of the first clinical examination, the following results were obtained.

Group	No. of dogs	Range of T3 (ng/ml)	Mean ± SD
OH	46	0.25 - 2.60	1.19 ± 0.50
P	77	0.03 - 3.25	1.10 ± 0.57
A	48	0.05 - 5.00	1.15 ± 0.71
EP	36	0.03 - 3.00	1.14 ± 0.55

The results of T3RIA for all groups are illustrated in Figure 11 .

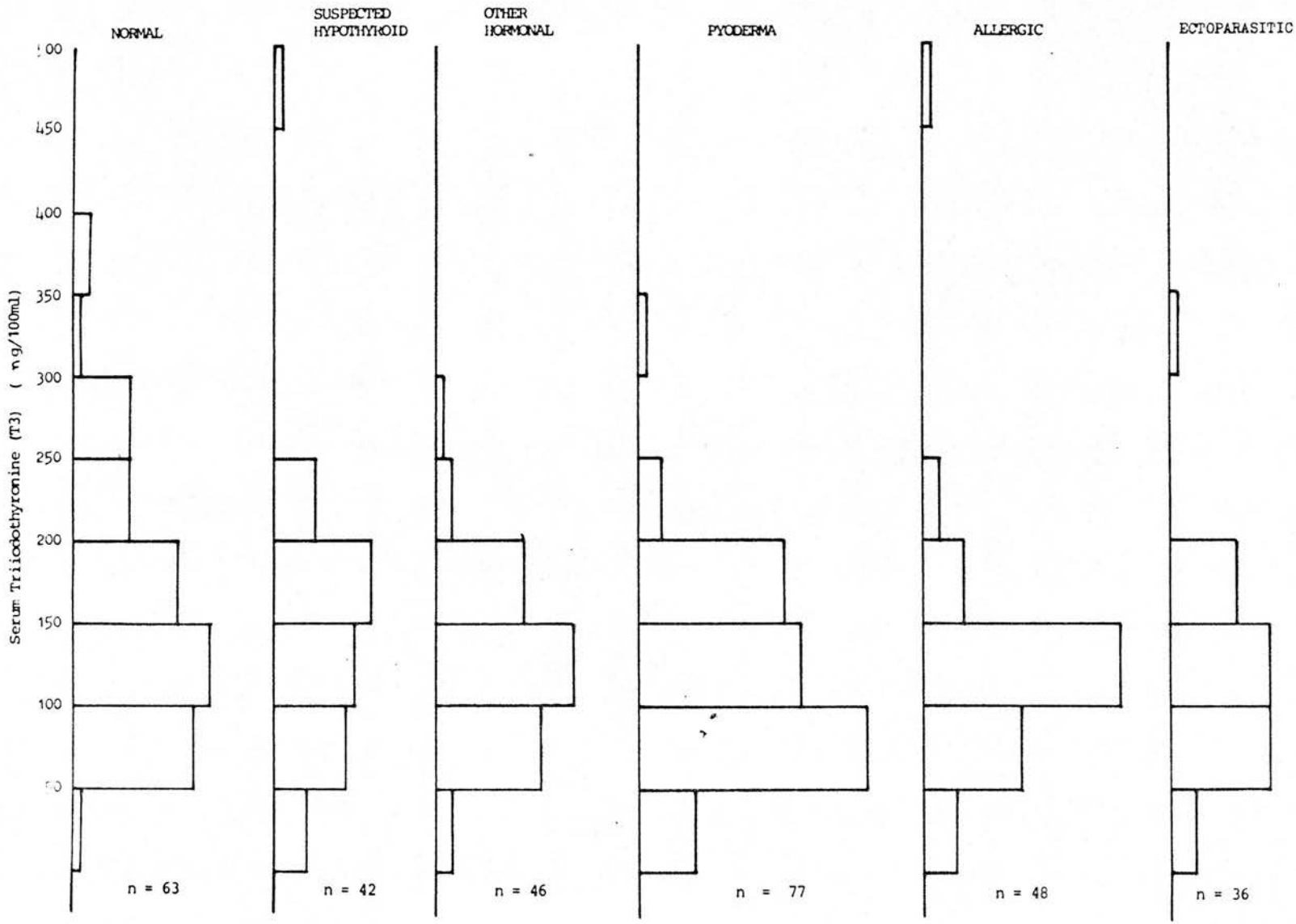


Figure 11 Comparative distribution of serum triiodothyronine in different dogs at time of first examination

VALUES OF SOME SERUM ENZYMES AND OTHER BLOOD CONSTITUENTS

In view of the results obtained, it is considered unnecessary to tabulate the results for individual dogs in respect of the values for SGOT, SGPT, SAP, plasma cortisol, blood urea and blood glucose. The mean and standard deviation of the values obtained for each enzyme or other blood constituent is set out by groups of dogs in Table 113 .

An analysis of variance was conducted on the values obtained for each substance assayed. Because of the very high standard deviations in Group OH for SGPT, SGOT and SAP values, this group was omitted from the analysis for these enzymes, but retained in the analysis for plasma cortisol, blood urea and blood glucose. For the same reason, Group HS was omitted from the analysis for blood urea only. No statistically significant differences were found between the groups in respect of any of the parameters. However, in the case of SAP and blood urea, when Duncan's new multiple range test was applied, the groups were found to have the following relationships of 2 subsets for each parameter.

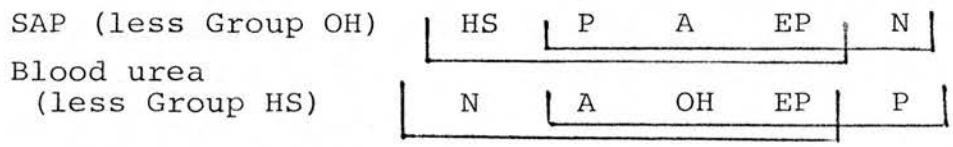


Table 113

Values of SGPT, SGOT, SAP and of resting cortisol, blood urea and plasma glucose, mean and standard deviation, in the six groups of dogs

Group	SGPT (IU/l)	SGOT (IU/l)	SAP (IU/l)	Cortisol resting (nmol/l)	Blood urea (mmol/l)	Blood glucose (mmol/l)
N	39.49 ± 26.28 (n = 35)	26.64 ± 19.69 (n = 35)	44.72 ± 32.01 (n = 35)	275.31 ± 209.90 (n = 61)	6.77 ± 1.89 (n = 5)	5.04 ± 0.37 (n = 5)
HS	52.84 ± 54.22 (n = 27)	20.33 ± 11.46 (n = 24)	111.66 ±169.65 (n = 29)	230.50 ± 203.81 (n = 17)	6.52 ± 6.81 (n = 13)	5.07 ± 0.93 (n = 17)
OH	116.45 ± 232.13 (n = 26)	37.43 ± 44.62 (n = 26)	411.39 ± 693.40 (n = 25)	242.48 ± 235.46 (n = 20)	5.13 ± 1.86 (n = 11)	5.25 ± 0.72 (n = 10)
P	51.07 ± 98.22 (n = 40)	22.64 ± 16.52 (n = 31)	59.82 ± 71.62 (n = 42)	258.53 ± 260.00 (n = 9)	4.44 ± 1.33 (n = 9)	5.24 ± 0.56 (n = 5)
A	41.39 ± 41.20 (n = 24)	24.78 ± 15.16 (n = 19)	94.80 ± 187.13 (n = 25)	191.38 ± 99.05 (n = 8)	4.22 ± 1.71 (n = 4)	5.26 ± 0.55 (n = 5)
EP	39.48 ± 22.88 (n = 17)	22.28 ± 14.82 (n = 17)	54.62 ± 86.26 (n = 19)	224.25 ± 124.64 (n = 4)	6.10 ± 2.47 (n = 4)	5.26 ± 0.41 (n = 2)

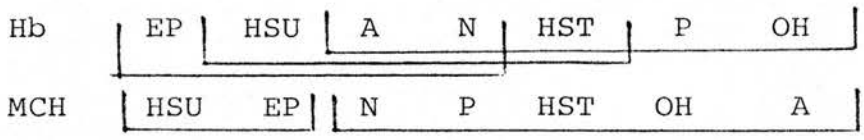
n = number of dogs on which the test was conducted

HAEMATOLOGICAL INVESTIGATIONS

Results

From the 307 dogs, a total of 406 blood samples were taken. Each sample provided 7 main haematological parameters and the differential cell counts, giving 12 items per sample, a total of some 5,500 individual results. These data were tabulated but because of their extensive nature, the tables are not presented in the thesis. From this material summaries have been prepared in tabular form.

Table 114 sets out the range of values obtained for the 7 main parameters. Values are given in Table 115. The mean and standard deviation for the analysis of variance was conducted on the mean and standard deviation values, and this information is also given in Table 115. The only parameters having statistical significance of the variance ratio were the haemoglobin and mean corpuscular haemoglobin values. Using Duncan's new multiple range test, it was ascertained that the significant subsets were as follows:



Normal Dogs

No haematological abnormalities were detected within the group. No dog was anaemic.

Table 114 Ranges of haematological values in all groups of dogs

Group	No. of dogs	RBC $\times 10^{12}/l$	PCV l/l	Hb g/dl	MCV fl	MCHC g/dl	MCH pg	WBC $10^9/l$
Normal (N)	49	5.19- 8.96	0.36- 0.60	11.90-23.00	60.10-86.10	27.60-40.60	20.40-29.80	4.50-29.80
Hypothyroid, suspected, untreated (HSU)	33	4.73-10.46	0.31- 0.62	9.80-21.60	41.22-77.72	29.10-39.20	13.03-28.13	6.50-24.70
Hypothyroid suspected treated (HST)	12	4.96- 7.62	0.40- 0.63	13.60-22.90	61.64-85.50	34.0 -40.40	22.42-30.64	7.20-19.20
Other Hormonal (OH)	44	4.16- 9.34	0.27- 0.60	9.50-21.40	60.50-84.10	31.40-46.80	21.90-34.50	5.50-27.20
Non hormonal Pyoderma (P)	80	4.44- 8.90	0.33- 0.60	11.50-21.90	51.8 -87.80	25.10-40.20	16.90-33.50	5.40-27.70
Non hormonal Allergic (A)	54	4.77- 8.47	0.34- 0.58	12.0 -20.50	58.50-84.80	32.40-45.40	21.30-32.50	6.60-29.10
Non hormonal Ectoparasitic (EP)	35	1.80- 9.35	0.10- 0.63	3.0 -22.30	55.60-86.70	30.00-38.80	16.70-29.40	7.10-30.70

Table 115 Mean and standard deviation (x±sd) of haematological values and their variance ratio in all groups of dogs

Group	No. of dogs	RBC $x\ 10^{12}/l$ x ± sd	PCV l/l x ± sd	Hb g/dl x ± sd	MCV fl x ± sd	MCHC g/dl x ± sd	MCH pg x ± sd	WBC $10^{9}/l$ x ± sd
Normal (N)	49	6.79±0.91	0.47±0.06	17.13±2.42	70.48±5.77	35.90±2.05	25.25±1.95	12.97±6.21
Hypothyroid suspected untreated (HSU)	33	6.91±1.20	0.46±0.06	16.18±2.83	67.38±7.23	35.04±2.22	23.57±2.77	12.62±3.87
Hypothyroid suspected treated (HST)	12	7.08±0.99	0.49±0.05	17.90±2.36	70.96±6.79	35.80±1.78	25.39±2.19	12.62±4.19
Other Hormonal (OH)	44	6.92±0.98	0.48±0.06	17.51±2.32	70.40±5.26	36.14±2.15	25.42±2.18	13.67±4.96
Non-hormonal Pyoderma (P)	80	6.97±1.02	0.48±0.06	17.47±2.36	70.21±5.85	35.84±2.28	25.29±2.14	13.69±5.06
Non-hormonal Allergic (A)	54	6.66±0.82	0.47±0.05	16.89±1.98	72.01±6.01	35.43±1.91	25.54±2.10	13.45±4.56
Non-hormonal Ectoparasitic (EP)	35	6.48±1.28	0.45±0.9	16.0±3.34	70.04±6.69	35.15±2.28	24.58±2.42	14.34±5.68
Variance ratio		0.26	0.06	2.62*	2.02	1.47	3.61**	0.49

* P<0.05> 0.01 ** P< 0.01

Cases of Suspected Hypothyroidism

Of the 33 dogs which had not previously been given thyroid therapy, 7 cases were sampled once and 26 cases had more than one blood sample taken. Treatment was instituted after the first sample was taken. Some form of abnormality was present in the haemogram of 10 of these dogs, as follows.

Case HS2 15 blood samples examined in 8 months. First examination showed early and intermediate normoblasts and a slight microcytic anaemia with slight hypochromia: 4.86 RBC x 10^{12}/l; PCV 0.32 l/l; Hb 10.4 g/dl. At examinations 3 and 8, there was slight to moderate polychromasia.

Case HS3 3 examinations 6 weeks. At examination 2, slight anisocytosis and polychromasia.

Case HS5 7 examinations in 9 months. At examination 5, a very few normoblasts.

Case HS7 15 examinations in 15 months. At examination 2, slight anisocytosis and poikilocytosis.

Case HS8 13 examinations in 27 months. At examinations 11 and 12, slight anisocytosis and polychromasia.

Case HS9 12 examinations in 6 months. At examinations 1, 5 and 6, the plasma was grossly lipaemic, causing sufficient turbidity to render estimation of Hb impossible. At examination 6, a chylomicron layer was present. At examination 7 there was slight polychromasia and anisocytosis.

Case HS11 6 examinations in 6 months. At first examination, moderate hypochromia and polychromasia, occasional normoblasts; 7.52 RBC x 10^{12}/l; PCV 0.31 l/l; Hb 9.8 g/dl.

Case HS26 2 examinations in 1 month. At first examination, slight hypochromia and normocytic anaemia; 4.73 RBC x 10^{12}/l; PCV 0.33 l/l; Hb 12.40 g/dl.

Case HS27 5 examinations in 8 months. At examination 5, marked hypochromia, anisocytosis and poikilocytosis; 5.28 RBC x 10^{12}/l; PCV 0.27 l/l; Hb 8.0 g/dl.

Case HS33 7 examinations in 19 months. At examination 6, the serum was very lipaemic.

Of 11 dogs which had previously received thyroid therapy, 3 were blood-sampled once and 8 on a number of occasions. Treatment was continued. Abnormalities of the haemogram were present in 5 cases, as follows.

Case HS10 11 examinations in 22 months. At examination 7, slight polychromasia.

Case HS13 9 examinations in 28 months. At first examination, very few normoblasts.

Case HS31 4 examinations in 16 months. At first examination, a slight macrocytic, normochromic anaemia: 4.9 RBC x 10^{12}/l; PCV 0.40 l/l; Hb 13.6 g/dl.

Case HS35 4 examinations in 2 months. At examination 2, evidence of increased platelet formation.

Case HS37 2 examinations in 1 month. At first examination, slight polychromasia and a few normoblasts.

Dogs with 'Other Hormonal' Conditions

Blood samples were examined once only. The following

features were noted in the 6 cases indicated.

Case OH1 Slight polychromasia, occasional late and intermediate normoblasts.

Case OH7 Slight anaemia, 4.16 RBC x 10^{12}/l; PCV 0.27 l/l; Hb 9.50 g/dl.

Case OH9 Moderate hypochromasia.

Case OH18 Lipaemic serum, chylomicron layer.

Case OH25 Slight anaemia, 4.19 RBC x 10^{12}/l; PCV 0.33 l/l; Hb 11.30 g/dl.

Case OH43 Chylomicron layer.

Dogs with Non-Hormonal skin conditions

Dogs with Pyoderma

Eighty dogs with pyoderma had haematological investigations conducted on one occasion. The following variations from the normal were noted in 10 cases.

Case P3 Increased platelet formation and a few normoblasts present.

Case P4 Moderate macrocytosis, occasional late and intermediate normoblasts; slight normocytic, normochromic anaemia: 4.44 RBC x 10^{12}/l; PCV 0.36 l/l; Hb 12.3 g/dl.

Case P13 Some monocytes showed vacuolation.

Case P25 Slight anisocytosis and polychromasia; occasional vacuolated monocytes.

Case P30 Slight anaemia; 4.75 RBC x 10^{12}/l; PCV 0.36 l/l; Hb 12.9 g/dl.

Case P51 Occasional late or intermediate normoblasts.

Case P54 Occasional vacuolated monocytes. Slight anaemia: 4.45 RBC x 10^{12}/l; PCV 0.33 l/l; Hb 11.50 d/gl.

Case P55 Slight anaemia: 4.99 RBC x 10^{12}/l; PCV 0.35 l/l; Hb 12.6 g/dl.

Case P57 Slight anisocytosis and polychromasia; late normoblasts.

Case P67 Increased platelet formation.

Dogs with Allergic Skin Conditions

Four of the 54 dogs in this group had some alteration from the normal haematology.

Case A7 Plasma lipaemia and chylomicron layer rendered estimation of this impossible.

Case A22 Moderate anisocytosis, polychromasia, occasional late and intermediate normoblasts.

Case A45 Monocytes vacuolated.

Case A56 Slight anaemia: 4.77 RBC x 10^{12}/l; PCV 0.35 l/l; Hb 12 g/dl.

Dogs with External Parasitism

Four of the 35 dogs in this group had some alteration from the normal haemogram.

Case EP9 Slight anisocytosis and polychromasia.

Case EP12 Marked anaemia: 3.91 RBC x 10^{12}/l; PCV 0.29 l/l; Hb 9.9 g/dl.

Case EP29 Hypochromia; a few macrocytic RBC.

Case EP43 Moderate micro- and macro-cytosis, slight

D J S C U S S I O N

anisocytosis, a few early normoblasts, some vacuolated monocytes, marked anaemia: 1.80 RBC x 10^{12}/l; PCV 0.10 l/l; Hb 3.0 g/dl.

All Groups

The means and standard deviations of the total leucocyte counts did not differ significantly between the group (see Table 115). If 20 x 10^9/l be taken as indicative of a mild leucosis, the different groups had the following numbers in that category. Very few of the cases had counts over 30 x 10^9/l.

Normal group	5 cases	in 49	1:10
HSU group	8 cases	in 34	1:4
HST group	0	in 11	0:11
OH group	4	in 44	1:11
NH,P group	11	in 80	1:7
NH,A group	5	in 54	1:11
NH,EP group	5	in 35	1:7

Taking 6 x 10^9/l as the lower end of the normal range, only one dog, N27, a member of the normal group, had less, namely 4.5 x 10^9/l.

It is of interest that the HSU group had the proportionately greatest number of cases with high (albeit only moderately so) total leucocyte counts, followed by the non-hormonal groups with pyoderma and external parasitism. As Schalm (1975) has indicated the devitalised or infected skin may be the cause of these changes. However, as already noted, there were no significant differences between the groups in respect of total leucocyte counts and this matter will not be discussed further.

CLINICAL OBSERVATIONS

Clinical comparisons will be made in the first instance between the HS group and the case series reported by others and, secondly, with the dogs of other groups investigated by the writer.

The most frequently observed clinical sign in the HS group was alopecia which affected 39 dogs (83%) with approximately equal numbers, 21 (44.7%) and 18 (38.3%) being affected with bilaterally symmetrical alopecia and asymmetrical alopecia, respectively. Alopecia is a well recorded finding but it has not usually been regarded as being the most common sign, for example Capen, Belshaw and Martin (1975) mention that it develops in 50-60% of hypothyroid dogs. On the other hand, Lievre (1976) accorded it first place with 76% in her review survey (Lievre summarised the relative frequency of various clinical signs in 51 cases reported by 4 other authors up to 1966 and reported on 16 cases in her own series, a total of 67 which will be referred to as Lievre's review survey).

In the present HS series, the main sites affected were on the lateral aspect of the trunk, namely the flank 19 times, 40.4%) and the sides of the chest (9 times, 19.1%) followed by the dorsal surface with, starting caudally, the lumbo-sacral region (9 times, 19.1%), the lumbar region (4 times, 8.5%), the dorsum (8 times, 17.0%), and the withers (3 times, 6.4%). Thus, the sides with 28 (56%)

appearances in the list and the back with 24 (51%) appearances, are important areas from the viewpoint of the occurrence of alopecia. The ventral aspect of the trunk was also affected, namely the belly (6 times, 12.8%) and the sternum (4 times, 8.5%) but the groin was only affected once and the axilla was not clearly identified as being affected. Of the limbs, only the hind legs were affected, the thigh (6 times, 12.8%), the posterior aspect of the hip (4 times, 8.5%)and the other upper parts of the leg and hip (4 times, 8.5%). The tail or tail head was affected in 4 dogs.

The neck was affected in 3 dogs (6.4%) and one of these cases was also affected on the ears and head. One case was affected on the face but not on the head or ears.

These sites have all been referred to by other authors although it is believed that a detailed account of the distribution in a series such as the present one is not common. Others have considered that the neck and ear flaps are commonly affected but that was not the present finding, although they are in agreement with the opinion of others that the face and lower parts of the legs are rarely affected.

Sixteen cases (34%) had sparse, rough, dry coats compared with the 12 cases in the series of 13 reported by Belshaw and Rijnberk (1977).

As Bush (1969a) and others have stated, veterinary attention is usually sought because of changes in the dogs'

skin and coat, although Muller and Kirk (1969) note that not all hypothyroid dogs have skin lesions, and according to Belshaw (1971) up to one-third of the cases do not have grossly visible skin lesions on first examination. The data presented here refer to the first examination. Skin lesions, as distinct from alopecia and other coat alterations, were manifested in a variety of ways of which the most frequent was inflammation in 29 (61.7%) of the HS group. The dermatitis cases included those with otitis externa (8), conjuctivitis (2), lichenification (4), seborrhoea (1 of 3 cases), comedones (2), hyperkeratosis (1 of 2 cases), and scaliness (1 of 2 cases), a total of 19 (40.4%). In the remaining 10, the dermatitis was very mild and causes could not be assigned. It is, of course, well recognised that the debilitated skin of hypothyroid cases is prone to secondary disorders, including infection. Not all of the HS series were examined bacteriologically, but in 12 cases from which skin cultures were made because infection was considered to be present, Staph. aureus was isolated.

That the dermatitis was frequently mild is confirmed by the fact that only 10 (21.3%) of the dogs exhibited pruritus. All of 10 cases, except one to which no cause could be assigned, were associated with 3 cases of otitis externa and six non-specific form of dermatitis.

Pruritus is not generally present in hypothyroidism and, when it does occur, it is due to factors other than the

hypothyroidism (Goyings et al., 1962; Mallo, 1966) such as seborrhoea or secondary infection. These are fairly frequent, slow healing complications according to Ojemann (1940), Bush (1969a), Ihrke (1979) and others. The present cases, in which pruritus was evident, also appear to have been, to some extent, of long duration as in 6 of the 10, hyperpigmentation had occurred. This is indicative of long-standing lesions (Coffin and Munson, 1953; and many others). Theran and Thornton (1966) consider that hyper-pigmentation occurs in less than half of cases, but Belshaw and Rijnberk (1977) reported it in 10 (77%) of 13 cases. In the present series it was present in a total of 19 dogs (40%) which is in keeping with the 34.3 reported by Lievre (1976) in her review series. No case of acanthosis nigricans was observed in the HS group.

Hyperkeratosis is regarded as a constant finding by Martin and Capen (1979), although Theran and Thornton (1966) consider it to affect less than half of cases and Lievre (1976) gives it an incidence of 40%. In the HS group, hyperkeratosis and scaliness were only recorded twice each (4 times, 8.5%). Lichenification (4 times) and seborrhoea (3 times) were also recorded. These 11 records referred to 9 dogs. Lichenification and seborrhoea may also be associated with scaliness (Goyings, 1961-62; Schalm, 1975) or, in the case of seborrhoea, with oiliness of the hair and skin (Chester et al., 1974; Schalm, 1975).

Otitis externa has already been mentioned, and had an

incidence of 8 cases (17%). This can hardly be regarded as a common occurrence although it has been commonly associated with hypothyroidism by Goyings et al. (1962), Munson and Belshaw (1966-67) and Muller and Kirk (1969, 1976).

Many authors e.g. Borgman and Reineke (1950), Meier and Clark (1958), Freudiger (1960) and others subsequently, have regarded thickening of the skin as an important feature. Belshaw and Rijnberk (1977) observed it in 11 of 13 cases. In the present series it was clinically present in 10 dogs (21.3%) including one with a puffy face. However, as is discussed elsewhere in the thesis, when measurements of double fold skin thickness were made using callipers at a number of sites, there was no significant difference in skin thickness between the groups of dogs except that the skin of the groin was frequently thicker in the HS and OH groups than in the other groups. In the HS group, the skin was considered to be thinner than normal in 2 cases (4.3%).

The denuded skin of the HS dogs was cool on palpation in 5 cases (10.6%), a matter which had been commented on by Goyings (1961-62), Moser (1966) and also by other authors more recently.

It is generally agreed that cases tend to have an insidious onset and are not usually presented at an early stage (e.g. Rijnberk, 1971, 1974) and that was also the situation with the suspected cases reported here.

While most of the present cases were presented because

of alopecia (39 cases, 83%) almost as many were lethargic and easily tired on exercise (36 cases, 76.6%). Generally, the presence of the latter sign was less commonly commented on by the owners in the first instance. Although sleepiness (8 cases, 17%) was recorded as a separate feature in the present cases, this was simply regarded as a further indication of lethargy and 5 dogs so described are included in the lethargic category. Belshaw and Rijnberk (1977) recorded 100% history of lethargy in their series of 13 cases, which is a higher proportion than that recorded in the HS group. However in her larger review survey, Lievre (1976) reported only 48% of cases to be lethargic.

The HS dogs were generally quiet and docile to handle and took less interest in the strange surroundings of the Clinic than one would expect. This manifestation of apathy has been commented on by a number of workers from Meier and Clark (1958) onwards. One of Rijnberk's (1971, 1974) series of six cases was exciteable whereas only 2 of the present 47 were. Maahs (1958-59), Freudiger (1960, 1962), and Kral and Schwartzman (1964) have occasionally encountered cantankerous cases but that was not the present experience. Belshaw (1971) regards the physical lethargy and dull mental attitude as being amongst the most frequent and prominent signs to the extent that he places them above alopecia or obesity. The present series confirms the importance of lethargy as a clinical feature but does

not place it above alopecia.

Obesity is discussed elsewhere in the thesis, with body weight and, while the HS series contained some 79% of overweight dogs, they were not all obese in the sense of being grossly fat or overweight. Nonetheless, Belshaw and Rijnberk (1977) did refer simply to overweight as occurring in 59% of their series of 13 cases, while in her review series, Lievre (1976) refers to obesity as affecting 42% of cases. Ekman et al. (1968) refer to pronounced obesity. In the present series, the basis for the decision was the standard weight of the breed and it is likely that, on this relatively less subjective ground than palpation and inspection, a higher incidence of overweight would be established. Accordingly, at present, it is not certain that, in a series of longstanding and other cases, lethargy will be more frequently present than alopecia and the latter than obesity. However, it is reasonable to accept that cases in the early stages of development are less likely to show skin and coat changes or weight increases and, correspondingly, are more likely to exhibit lethargy. The differences, due to the stage of the disease at which cases are first presented to a veterinary surgeon, will affect the incidences.

It has been noted elsewhere in the thesis that weight gain cannot simply be ascribed to increase in appetite for while, in the present series, 8 dogs (17%) were greedy, and 3 (6.4%) lacked appetite, the remainder were not, in

the owners' opinion, abnormal in this respect. It may be concluded that as the appetite tends to remain normal but that the dogs become increasingly lethargic, the demand for usable energy diminishes as part of the general syndrome of lowered metabolic activity associated with hypothyroidism (e.g. Rijnberk, 1971; Kallfelz, 1977) and so the dogs become overweight.

Amongst the altered patterns of behaviour, thermophilia deserves mention. Seeking warmth was recorded in 6 (12.8% of cases. Although it is widely reported as occurring, Munson and Belshaw (1966-67) and Bush (1969a) note that this is a difficult matter to assess. Numerical data are provided by Belshaw and Rijnberk (1977) who report it in 12 of their 13 cases (92%) and they place it second only to lethargy in their hierarchy of signs. It may be that owners attending the Clinic in Edinburgh were less observant but it has also to be noted that in the Edinburgh area the environment is cold for much of the year and no doubt many owners considered it not abnormal for their pets to seek warmth.

It is to be regretted that with regard to the history of reproductive function and behaviour, matters much discussed by others in relation to hypothyroidism, the present writer was unable to obtain reliable information. Regarding male libido, the owners of male dogs either did not know how their dogs behaved when turned loose or the dogs were kept so much under control that no opportunity

was afforded the owners of making observations.

Generally, the bitches of the HS group were also restrained when in oestrus. However, of the 28 entire females in the HS group, 3 manifested false pregnancy and 2 had gynecomastia at the time of first examination, i.e. 17.9% of the entire females had some obvious derangement of the reproductive tract or mammary glands. Without making distinctions between the sexes, Lievre (1976) reports 22% of reproductive dysfunction.

Although others have reported on muscular and joint problems in hypothyroid dogs, such were not recorded in the present series.

Constipation occurred in 1 and diarrhoea in 3 of the HS group. It is doubtful if these observations are meaningful, although the occurrence of intermittent constipation has been noted by Freudiger (1960) and others subsequently. Rijnberk (1971, 1974) stated that it is a fairly common finding in human hypothyroidism, but did not observe it in his 6 canine cases. Later, however, he (Belshaw and Rijnberk, 1977) recorded it in 2 of 17 cases. Capen et al. (1975) consider it to be uncommon. Occasionally mild diarrhoea occurs but Munson and Belshaw (1966-67) and the later writers who comment on this, do not give its incidence in their series.

The present purpose is not to discuss the results of clinical examinations of the dogs in the OH and NH (P, A and EP) groups for their own sake. Instead it is intended

to discuss the results in comparison with those obtained in the HS group as a part of the consideration of differential diagnosis.

In the 47 OH cases, alopecia was the most frequent finding in this rather diverse group and it was present in 26 (55%). It was asymmetrical (15 cases, 32%) in more dogs than it was symmetrical (11 cases, 23%). Group OH may be divided into 2 sections, the first containing dogs with Sertoli cell tumours (7), Cushing's-like syndrome (6), iatrogenic Cushing's disease (5) and cases regarded as hormonal alopecia relatively uncomplicated by other skin disturbances (5), a total of 23. The other contains the remainder of group OH, i.e. 24 dogs. In the first section 14 (60%) had alopecia with the distribution equally symmetrical and asymmetrical. Also in this section were the two cases of calcinosis cutis and all 5 cases of pendulous abdomen (pot belly). Three of the latter were associated with the 6 cases of Cushings-like disease. The 24 other dogs had 12 cases (50%) of alopecia, 4 (16.7%) and 8 (33.3%) being symmetrical and asymmetrical respectively. The occurrence of alopecia, often bilaterally symmetrical, is well recognised in Sertoli cell tumour cases, Cushing's syndrome and hypoandrogenism in male dogs and in post-oestral and post parturient bitches (Coffin and Munson, 1953; Meier and Clark, 1958; Walton, 1965; Bush, 1972a; Kelly and Darke, 1976).

The sign next in importance to alopecia was pruritus

(18 cases, 38%). These and the other clinical findings are set out in Table 30. Table 116 compares the incidence of various clinical signs in the HS group and the OH group. Many clinical signs are common to the 2 groups but there are two main significant differences. These refer to alopecia ($P < 0.05$) and lethargy ($P < 0.001$). These clear distinctions between the 2 groups are noteworthy with both characteristics being significantly more frequent in the HS group than in the OH group. From the crude data, lethargy is 5 times more likely to be associated with suspected hypothyroidism than with other hormonal disorders and the frequency of alopecia in the HS group is to the OH group as 3:2. A third common feature, namely inflammation of the skin, which is often of the mildest nature, is only marginally ($P > 0.05$) more likely to occur in the HS group although the absolute numbers and percentages would suggest otherwise as a first impression. There are no significant differences between any of the other findings, including, for example, such relatively frequently occurring dermatological features as hyperpigmentation, sparse coat, thick skin and pruritus. Apart from lethargy which has already been noted to be highly significantly more likely to occur in the HS group, there is no significant difference in behavioural matters such as thermophilia, quality of appetite and the occurrence of nervousness.

The large 'non-hormonal' group consists of 3 groups. Group P, consisting of 99 pyoderma cases, is particularly

Table 116

Comparison of incidence of certain clinical signs in the HS and OH groups

Clinical sign	Group HS		Group OH		Chi-square
	No.	%	No.	%	
Alopecia	39	83	26	55	7.181 **
Lethargy	36	77	7	15	33.605 ***
Skin inflamed	29	62	17	36	5.151 *
Hyperpigmentation	19	40	13	28	1.184
Dry, sparse rough hair	16	34	13	28	0.199
Thick skin	10	21	11	23	0.000
Pruritus	10	21	18	38	2.500
Sleepiness	8	17	5	11	0.357
Polyphagia	8	17	7	15	0.000
Otitis externa	8	17	4	9	0.860
Thermophilia	6	13	2	4	1.230
Enlarged lymph node	5	11	6	13	0.000
Polydipsia	5	11	4	9	0.000
Skin cold	5	11	2	4	0.617
Easily epilated hair	4	9	6	13	0.112
Lichenified skin	4	9	1	2	0.845
Anorexia	3	6	2	4	0.000
Anal sac impacted	3	6	8	17	1.647
Comedones	2	4	1	2	0.000
Diarrhoea	3	6	2	4	0.000
False pregnancy	3	6	5	11	0.137
Cough	2	4	1	2	0.000
Scaliness	2	4	8	17	2.800
Gynecomestia	2	4	5	11	0.617
Pot belly	2	4	5	11	0.617
Seborrhoea	3	6	6	13	0.500
Nervousness	2	4	2	4	0.000

P*** < 0.001

P** < 0.01

P* < 0.05

characterised by dermatitis. While the incidence of dermatitis in Group HS is 61.7%, in Group P it is 100% i.e. 99 cases. However, the main difference does not lie in the incidence but in the nature of the process. In Group P, inflammation of the skin can be acute (41), severe (39) and generalised (43) and over half of the cases are pruritic (55). The frequency of aural (24) and inter-digital (13) inflammation is also different from that in the HS group where they are 17% and nil respectively. (The number associated with Group P refers to numbers of cases in 99; to convert these to percentages offers no advantage).

A further distinction is noted in respect of alopecia, which is 83% in Group HS and only 11 in Group P.

Even although Group P has the higher incidence of dermatitis, the frequency of thickening of the skin (8) is less than that of Group HS (21.3%) and hyperpigmentation is also less in Group P (28) than in Group HS (40.4%). No cases of acanthosis were recorded in the HS group but there were 6 cases in Group P and this group also had a greater incidence of scaliness (12) than the HS group (4.3%).

Group A, cases of allergic skin disorders, consisted of 57 dogs. All of Group A, but only 61.7% of Group HS, had dermatitis. Again, the main feature was the nature of the inflammation which tended to be mild in the HS group but was otherwise in Group A in which pruritus and erythema were both at 98.2%, compared with 21.3% and 10.6% respectively in the HS group. Furthermore, the dermatitis

was acute (36.8%) and severe (49.1%) in Group A and did not follow any symmetrical pattern. An important indication of the severity of the pruritus in Group A was that 45.6% of the dogs bit at and pulled the skin and coat of affected areas, a feature not recorded in any HS case. Despite this, alopecia was manifested in only 19.3% of the A group, compared with 83% of the HS group. Generally, the dogs of Group A were not lethargic (1.8%) whereas this was a very important finding (76.6%) in Group HS.

The invariable feature which characterised the dogs of Group EP was the demonstration of external parasites. These 49 dogs had both pruritus and erythema and the 93.9% level compared with 21.3% and 10.6% respectively in the HS group. Inflammation of the skin, whether mild (24.5%) or severe (75.5%), acute (65.3%) or chronic (34.7%), generalised (59.2%) or localised (40.8%) was invariable, and its acute, severe nature distinguishes it from the rather mild dermatitis (61.7%) occurring in Group HS. Alopecia is 32.7% in Group EP compared with 83% in Group HS and it has no symmetrical distribution in the EP group.

The general clinical picture in the 2 groups is very different. The Group HS dogs tend to be lethargic but the dogs affected with external parasitism are not. They are active, scratching, restless dogs with 53.1% so affected by the pruritus that they bite and pull at their own skin and coat, One EP dog, with pale mucosa, and confirmed severe anaemia, was clearly a weak, severely

affected animal and it died.

A statistical analysis to compare the clinical findings in the HS group with those of the P, A and EP groups is not considered necessary. The real differences depend on a demonstration of the different nature of the lesions and clinical signs rather than on their comparative frequency, even although there are many marked differences in their incidence.

Preliminary differential diagnosis between suspected hypothyroidism and other suspected hormonal disorders can be difficult. In the present investigation both the HS and the OH groups contained 47 dogs. In Group HS, alopecia, lethargy and overweight were recorded 39, 36 and 38 times. The corresponding figures for Group OH were 26, 7 and 16. As is indicated elsewhere, there is a statistically significant difference between the 2 groups for each of the 3 parameters.

A review of the clinical findings of the individual dogs reveals that in Group HS, 32 cases of alopecia also manifest lethargy, 31 cases of alopecia are also overweight, 26 cases of alopecia are also both lethargic and overweight, and 30 cases of lethergy are also overweight. The situation is very different with Group OH. Only 1 case of alopecia was associated with lethargy, only 6 cases of alopecia were also overweight, only 1 case of alopecia was both lethargic and overweight and 4 lethargic dogs were overweight.

Since both groups were the same size, comparison is facilitated. In every 100 dogs suspected of hypothyroidism or other hormonal disturbance, which have alopecia plus lethargy plus overweight, $\frac{26 \times 100}{26 + 1} = 96$ are likely to be cases of hypothyroidism and $\frac{1 \times 100}{26 + 1} = 4$ are likely to have other hormonal disorders.

This analysis is based only on the present, clinical assumptions. If only 2 parameters are chosen, again against a background of suspecting hormonal dysfunction from the history and clinical findings generally, the following guide lines appear.

Parameters	HS %	OH %
Alopecia + overweight	83.8	16.2
Alopecia + lethargy	97.0	3.0
Lethargy + overweight	88.2	11.8

It is evident from the above, as from the statistical analysis given elsewhere, that in dogs, when other diagnostic possibilities have been excluded and where hormonal dysfunction is suspected to be the cause of the clinical manifestations, the presence of a combination of alopecia and lethargy is very suggestive of hypothyroidism.

The real problem of differential diagnosis at the preliminary clinical level remains in respect of dogs which do not show any pair of alopecia, lethargy or overweight. On the basis of the data obtained in the clinical part of the present study, this includes 6 dogs in Group HS and 37 in Group OH. Thus, on clinical grounds, the problem of

making a preliminary diagnosis of suspected hypothyroidism should be considerably less than that of making one of other hormonal disturbance. However, for example, the presence of pendulous abdomen and calcinosis cutis advances the likelihood of Cushing's-like disease and palpable change in the testes increases that of Sertoli cell tumour. Against such a background, the selection of the appropriate laboratory tests is likely to be more meaningful and their results more amenable to correct interpretation.

BODY WEIGHT

The dogs with suspected hypothyroidism contained a significantly higher proportion of overweight dogs than the other groups. Generally, while others have referred to the importance of overweight as a finding in many, but not all, cases of hypothyroidism, they have, when reporting in numerical terms, referred to obesity and by this gross overweight may be implied. For example Meier and Clark (1958) recorded obesity in 9 of 38 cases (23.7%). However, while the present discussion does include some dogs with obesity, the characteristic considered is an increase in weight above the normal weight for the breed. Thus, the 78.7% of cases in the present series of 43 weighed dogs with suspected hypothyroidism is in keeping with the 61.5% of overweight dogs reported by Belshaw and Rijnbeck (1977) in 13 cases. Goyings (1961-62) had described 16 of his 27 cases (59%) as obese.

Meier and Clark (1958) and Goyings (1961-62) recorded obesity more frequently than alopecia in their cases. However, in the present series of cases of suspected hypothyroidism, 39 of 47 cases (83%) had alopecia, a marginally higher proportion than the 79% of cases of overweight.

In the present investigation, 45% of 236 dogs were overweight. If the cases of suspected hypothyroidism are omitted, 35.8% were overweight. This is in close agreement with the 34% of obese dogs recorded in a survey of 1134 dogs conducted by Edney (1972).

In the present investigation, detailed enquiries were made of the owners when they presented their dogs at the Clinic about the diet provided and the dogs' eating habits. Items fed included proprietary dog foods (meats, meat mixtures, biscuits) and such items as table scraps, beef, mutton, chicken, fish, eggs, sausages, bone marrow, liver, heart, tongue, tripe, milk, cheese, mixed vegetables, fruit, brown bread, sweet biscuits, sweets and breakfast cereals. No simple pattern emerged but it did appear that most dogs were receiving an adequate mixed diet with reasonable amounts of protein, fats, carbohydrates, minerals and vitamins. Some dogs received supplemental vitamins and minerals.

Most owners reported that their dogs had good appetites and some described it as very good, excellent or greedy. Other descriptions were moderate, could be better, occasionally poor or varying from time to time. Again, the information was not amenable to any precise analysis. While, in general, the description of the appetite appeared to match the dog's bodily condition, enquiry revealed that not all of the overweight dogs were greedy. It appeared that the hypothyroid suspected cases, which contained a significantly higher proportion of overweight dogs, included as well as some greedy dogs, others which had normal or poor appetites, and the impression was gained that overeating was not the only or even the main factor in their increased body weight. That an increased appetite is not necessarily

present in overweight dogs with hypothyroidism has been reported by others (Bryan, 1960; Hoffer, 1962; Theran and Thornton, 1966; Rijnberk, 1971; Martin and Capen, 1979), although Belshaw (1971) associated it with overeating.

The dogs' interest in exercise, an important factor in relationship to body weight when the diet is considered, is discussed elsewhere.

INCIDENCE

Breeds of Dogs with Suspected Hypothyroidism

Discussion

Both larger and smaller breeds are equally represented within the group. The incidence of spontaneous hypothyroidism within each breed is not established, as the distributions of breeds in local populations is not usually known. However, in the 12 year period 1964-1975, 686 dogs with various skin complaints were admitted to the Small Animal Clinic of the School and their breeds recorded. It is acknowledged that this is only a part of the Clinic population but it affords some indication of the frequency with which various breeds were presented. This is referred to as the selected population. Tables 117 and 118 set out the numbers of dogs of each breed encountered in the present series, for larger and smaller breeds respectively. The tables compare the numbers with the numbers of the same breeds in the selected population and the numbers are also given of dogs of other breeds in the selected population, for which there are no related cases of suspected hypothyroidism.

From Table 117 it can be seen that there were 22 dogs and 365 dogs of the larger breeds in the HS series and the selected population respectively,, a ratio of 1:16.6. On average this suggests that if no breed predisposition exists, about 1 dog in 16 or 17 of a given larger breed would be likely to be a case of suspected hypothyroidism. Of the breeds named in the table, it is

Table 117

Numbers of dogs of the larger breeds in the hypothyroid suspected cases (HS) and in the selected population (SP)

Breed	HS No.	SP No.	Ratio
Airedale	3	3	1:1
Boxer	1	18	1:18
Collie	1	85	1:85
Chow	1	2	1:2
Doberman	3	6	1:2
I. Setter	3	2	1:0.66
Labrador	8	82	1:10
P M D	1	-	
Spaniel	1	69	1:69
Alsatian		50	
G. Retriever		11	
Greyhound		8	
Others		29	
Totals	22	365	1:16.6

Table 118

Numbers of dogs of the smaller breeds in the hypothyroid suspected cases (HS) and in the selected population (SP)

Breed	HS No.	SP No.	Ratio
Cairn T.	4	24	1:6
Corgi	1	11	1:11
Dachshund	3	14	1:4.7
Lakeland T.	1	-	
Poodle	4	46	1:11.5
Scottish T.	2	14	1:7
S H F T	1	15	1:15
Shetland C.	1	11	1:11
W H W	4	33	1:8.3
York T.	2	7	1:3.5
K C S		5	
Pekinese		7	
Terriers, mixed breed		85	
Terriers, named breed		12	
Others		11	
Totals	23	295	1:12.8

evident that this is not generally the case. Of the breeds in the selected population with more than 16 representatives, the Labrador with a ratio of 1:10 is the only breed about which it may be said that its frequency in the HS group is unexpectedly high. The frequency in the Boxer (1:18) was such as might be expected, whereas in the collie and spaniel (1:85 and 1:69 respectively) it was very low, and in the Alsatian (0:50) there were suprisingly no cases.

There were 26 medium sized dogs in the selected population of which 13 were beagles. One beagle and one Tibetan terrier were included in the HS group.

Table 118 shows that there were 23 dogs and 295 dogs of the smaller breeds in the HS series and the selected population respectively; a ratio of 1:12.8, suggesting that about 1 dog in 12 or 13 of any given breed would be likely to be a case of suspected hypothyroidism. On this basis the following breeds may be considered to be overrepresented to a noticeable extent: Cairn terrier (1:6), Dachshund (1:4.7), Scottish terrier (1:7) and West Highland White terrier (1:8.25). The Corgi (1:11), Poodle (1:11.5), Shetland Collie (1:11) and fox terrier (1:15) are almost as expected.

In the selected population, there were 12 other terriers of named breeds and 85 terriers of mongrel type totalling 97. They might be expected to have some 7 or 8 associated cases of suspected hypothyroidism in a total of 47 cases. However, there were no such cases, suggesting that the incidence is

low in this type of dog despite its apparent frequency (mean 1:7.1) in other terriers such as Cairn, Scottish and West Highland White. It may be that these dogs are of sufficiently related type to form a group distinct from that consisting of the Border, Bedlington, Jack Russell, Maltese and Sealyham terriers which composed the 12 other named breeds of terrier. However, it is equally possible that the group of 12 is too small for any meaningful conclusion to be reached. Although in Table 118 , other terriers such as the Lakeland and Yorkshire have a very narrow ratio (mean 1:2:3) the actual numbers involved are too small to merit further discussion.

It is now appropriate to consider whether the incidence is greater in the larger breeds as has been suggested by others (e.g. Bush, 1972a, 1977, 1979; Belshaw and Rijnberk, 1977)..

There were 22 dogs of larger breeds in the HS group and 365 in the selected population, a ratio of 1:16.6, whereas there were 23 smaller dogs in the HS group and 295 in the selected group, a ratio of 1:12.8. The overall ratio was 47 HS: 686 selected population i.e. 1:14.6. This does not support the contention that the incidence is greater in the larger breeds.

In the present HS series, although statistical significance cannot be placed upon the figures, it appears that the breeds with an incidence clearly higher than the selected population numbers would suggest, were the Labrador

of the larger breeds and the Cairn, Scottish and West Highland terrier and Dachshund of the smaller breeds. Of these, the Dachshund is the only one to have been referred to by others to any extent, either as appearing more frequently in their case lists than would be expected or that it has a statistically higher incidence than other breeds. In summarising 91 cases reported by others, Lievre (1976) noted that the Dachshund occurred 11 times, and it occurred once in her own 16 cases. Rijnberk (1971) reported it as one of his 6 cases. Goyings et al. (1962) and Greene et al. (1979) also rate it as an important breed for hypothyroidism. In a very recent publication, Blake and Lapinski (1980) report a high percentage of low T4 readings in the Labrador in suspected hypothyroid cases. These workers were reporting on blood samples from 2,033 dogs of various breeds, submitted to a laboratory for the Micro-Dot T4 test. This appears to be in support of the present observation.

Others have emphasised the occurrence of hypothyroidism in spaniels. Goyings et al. (1962) reported 11 spaniels in their 50 cases, and Lievre (1976) found 17 spaniels to be affected in 91 cases reported by others. Her series of 16 cases did not include the spaniel. Bush (1972a, 1977, 1979) Muller and Kirk (1976), Belshaw and Rijnberk (1977) and Greene et al. (1979) also include spaniels amongst the large breeds in which the occurrence of hypothyroidism is noteworthy. In the present series, on the contrary, its occurrence was low at 1 case in 47 or in relation to the

selected population, 1:69.

In the 91 cases summarised by Lievre (1976) there were 8 beagles, but none in her own 16 cases. Goyings et al. (1962) also refer to its spontaneous occurrence in this breed. In the present series it occurred only once in 47 cases although this represents a ratio of 1:13 in the convention used here.

Lievre (1976) reported the poodle 4 times in 91 cases and in 5 of her own 16 cases. In the present series 4 of 47 cases were poodles or in the convention adopted in this section, 1:11.5. There seems to be agreement that the poodle is a breed at above average risk of hypothyroidism as is also the setter. The Irish setter in particular has been referred to by Bush (1972a, 1977, 1979), Muller and Kirk (1976), Belshaw and Rijnberk (1977) and Greene et al. (1979). Setters composed 6 of the 91 summarised cases and 2 of her 16 cases (Lievre, 1976).

In the HS series, there were 3 Irish setters in 47 cases although the ratio convention used here (1:0.66) refers only to this small number, it is evident that the I. setter also is at considerable risk of hypothyroidism. However Blake and Lapinski (1980) place it about the mean in their list.

In the HS series the Boxer did not feature prominently at 1 in 47 or as 1:18 in the selected population ratio. Lievre (1976) did not report its occurrence in her 16 cases although she records the Boxer 6 times in the 91 cases

already referred to.

In summary, if by breed incidence is meant the actual frequency with which the spontaneous disease appears in a breed, it is not possible to provide definite figures. It is however possible to note the proportions of the different breeds occurring in a given series and, furthermore, as in the present study, to relate the frequency of the disease's occurrence in a breed to, at least, a selected population.

Age of Dogs with Suspected Hypothyroidism

Discussion

The age range reported here i.e. of 2 dogs less than 6 months old and the remainder from 2 to 13 years with an average of 7.35 years (if the two youngest cases are excluded), is somewhat higher than that reported by Meier and Clark (1958) and Goynings et al. (1962) who gave the average as 5.7 and the range as 1.5 to 11 years, and by Rijnberk (1971), Bush (1972) and Belshaw and Rijnberk (1977) who gave ranges of 2 or 3 to 5 years. In the present series, dogs aged 7 to 13 years, i.e. middle-aged and older dogs, predominated by 29:18. Capen, Belshaw and Martin (1975) and Bush (1977) and Greene et al. (1979) also considered the incidence to be greater in this age group.

Lievre (1976) gave the mean age of first appearance of the disease in her 16 cases as 4.5 years with it appearing in male and female at 6.6 and 2.8 years respectively. In the HS series the mean age for the 14 entire males and 29 entire females at the time of the first examination by the present writer was 7.7 and 6.7 years respectively. However, the females showed both an earlier and a later peak, namely at 2-3 years and 7-9 years. It seems that Lievre's smaller series did not show this pattern. The present data do, however, suggest that females are likely to be affected at a younger age than males.

Muller and Kirk (1976) indicated that hypothyroidism

can occur at an earlier age in the giant breeds, a view that Bush (1979) has endorsed. In the HS series, giant breeds were relatively unimportant numerically but when the age pattern of the larger breeds (22 cases) is compared with that of the smaller breeds (23 cases), the average age at which the cases were first examined by the present writer was 5.8 and 8.0 years for the large and small breeds respectively.

Thus one may conclude that the disease can occur at any age but that the incidence increases with age being about one-and-a-half times more likely from 7 years of age than earlier. Females are likely to show signs earlier than males and dogs of the larger breeds are also likely to show signs earlier than smaller dogs.

These opinions have been reached from a study of the HS group alone. However, the relationship of age to disease merits further consideration which takes into account the other group. The age patterns of the other group are reported within the relevant section. In the N group of 68 normal dogs, the age of 62 was known. Of these, 7 were 7 years of age or more and 54 were younger than 7 years, a ratio of 1:1.7. The NH group contained 204 dogs of known age, the equivalent numbers being 53 and 151, a ratio of 1:2.8. In the OH group, there were 27 older and 20 younger dogs, a ratio of 1:0.7 and in the HS group the numbers were 29 and 18 respectively, a ratio of 1:0.6. Generally, these ratios indicate that, with increasing age,

ill health increases in frequency. Furthermore, the frequency of both suspected hypothyroidism (HS) and other hormonal disorders (OH) is similar in the older dogs, and is much greater in the older dogs, by a factor of approximately 4 than is the likelihood of their being affected by the skin complaints which affected the NH group. This is to some extent understandable as no protective immunity develops to hypothyroidism while it may to some of the conditions such as mange, and also to pyoderma, which affected some half of the NH group.

Sex of Dogs with Suspected Hypothyroidism

Discussion

The present study concerned itself with 4 groups of dogs, namely normal dogs, suspected hypothyroid cases, 'other hormonal' cases and dogs with other, non-hormonal skin conditions, a total of 367 dogs. Table 119 gives the percentage distribution by sex of the dogs under investigation, and also of the 'clinic population' referred to in Materials.

The Clinic population of 7,802 dogs and the dogs of the present study, other than the HS group, have a fairly close agreement on the proportions of entire male and female dogs. Both male and female neutered dogs comprise a larger proportion of the 4 groups of the present series overall than of the Clinic population. It is strikingly noticeable, however, that the ratio of male to female dogs, 1:2 in the HS group, is very different from that of the Clinic population, where the ratio is 1:0.8. The difference is statistically significant, $P<0.05$.

The females are 2.5 times more numerous in the HS group than would be expected from the Clinic population. While it is accepted that the Clinic population may not represent the true local population, it is not always clear what, if any, basis of comparison has been used by other workers. Others (e.g. Goyings et al., 1962; Bush, 1972

Lievre, 1976; Greene et al., 1979) found no difference in the proportions of male and female dogs affected. Lievre (1976) summarising the sex of 89 cases reported by others in the literature, prior to 1974, gave the ratio as 46 males to 43 females.

Castrated males and neutered females form a higher proportion of the HS group than of the Clinic population. While the actual numbers involved may be too small to merit detailed analysis, the trend is in keeping with the observation of Greene et al. (1979) that significantly more spayed females had hypothyroidism than would be expected from the numbers in their Clinic population. Maahs (1959) had expressed the opinion that it was more common in spayed bitches but it seems that this view lacked support until the report by Greene et al.(1979) and the present observation.

In a consideration of the proportion of male dogs and, conversely, of female dogs, in each of the groups studied, when all of the groups are considered the Chi-square test (Snedecor and Irvine, 1933) reveals a high degree of heterogeneity in respect of sex ($P<0.001$). When the HS group is removed, the test reveals no significant difference between the remaining groups, i.e. they are homogeneous in regard to sex. Thus, the proportions of male dogs in the HS group is highly significantly different from those in the other groups. This is set out in Table 120.

Table 121 sets out the proportional relationship

of the male and female dogs of the HS group to the other groups. The statistically significant difference ($P<0.01 >0.001$) reveals that the incidence of hypothyroidism is greater in female than in male dogs.

Table 119

The percentage and total numbers of the dogs in various groups

Group	Percentage of each sex				Total number
	M	Mn	F	Fn	
Clinic population	53.82	0.69	41.71	3.78	7,802
N,HS,OH,NH	48.23	3.00	42.23	6.54	367
N,OH,NH	50.94	3.44	39.38	5.94	320
HS	29.79	2.13	61.70	6.38	47

N: normal dogs
HS: suspected hypothyroid dogs
OH: other hormonal cases
NH: non-hormonal skin cases

M: male Mn:male neutered F: female Fn: female neutered

Table 120

The proportion of male dogs in the group

Group	No. of dogs	No. of male dogs	Percentage
N	64	36	56.25
HS	43	14	32.56
OH	39	21	53.85
P	94	58	61.70
A	45	22	48.89
EP	47	25	53.20

Group	Degrees of freedom	Chi-Square
All above	5	325.325***
All above less HS	4	2.3593

P*** <0.001

Table 121

The proportion of male and female dogs, comparing the HS group with the other groups

Group	No. of males	Percentage	No. of females	Percentage
HS	14	32.56	29	67.44
All other groups less HS	162	56.05	127	43.95

Group	Degree of freedom	Chi-square
All	1	7.380**

P** < 0.01 > 0.001

SKIN THICKNESS

Discussion

It is appreciated that extensive statistical analysis has been applied to measurements that do not have absolute accuracy because they are made by a manual method with calipers, and only to the nearest mm. However, every measurement was made by the same person (the present writer) who tried to maintain the same amount of pressure in each case.

As expected, the skin thickness varied from site to site in individual dogs and there were some breed differences (Hauck, 1949; Brunsch, 1956). However, all of the measurements by skin sites, by group of dog and by breed overlapped.

The literature, previously cited, contains numerous references to increased skin thickness in hypothyroidism but this was not found in the dogs examined in this experiment. The hypothyroid dogs had only one site, the groin, where the skin was significantly thicker than that of other dogs, and even then it did not differ statistically from that of the dogs with hormonal conditions other than hypothyroidism. This was not a breed effect, for the groin was not one of the sites which was significantly different in the different breeds. The skin thickness of the groin in some hypothyroid dogs was no greater than that of many dogs in the other groups. Thus, the difference

detected was a statistical one, but not a diagnostically dependable one by itself, i.e. the absence of skin thickening does not eliminate hypothyroidism whereas its presence is only meaningful when other more important signs are present.

Conclusions

The clinical observation that in hypothyroidism the skin may be thickened has not been supported at a statistically significant level except perhaps for one site which is also thickened in "other hormonal" conditions. It is evident that no reliance can be placed on skin fold thickness measurements to ascertain whether a dog is affected with hypothyroidism or other disease conditions.

STAGES OF HAIR CYCLE IN HYPOTHYROID AND OTHER DOGS

Discussion

The average percentage of hairs in the anagen phase of the 10 normal dogs examined monthly for one year was 23.7, 27.0, 19.8, 17.4, 15.6, 16.9, 16.7, 18.3, 19.8, 20.2, 20.4, 26.6 for the months from January to December respectively. That is, in south-east Scotland, the anagen percentage tends to be highest in the winter months of December, January and February, lowest in the late spring and early summer months of May, June and July, and occupy an intermediate position in the spring month of April, and from August to November, the late summer and autumn. Although the data are not numerous, being based on 12 counts on each of 10 dogs, they indicate a trend of one main period of relatively greater anagen activity, namely the winter months. However, there is no month when the average anagen frequency was more than 27%.

Accordingly, telogen predominated throughout the year.

This agrees in part with the findings of Al-Bagdadi et al. (1977) who also found an anagen peak of follicular activity in winter. However, they also reported a second one in summer. It should be noted, however, that unlike the dogs of Group One, A, reported here, Al-Bagdadi et al. were working with dogs that spent the day out of doors. This would affect the pattern of follicular activity, for, as Thomsett (1966) has stated, when dogs are kept in household conditions there may be little seasonal variation in hair loss.

Because of the occasional manner in which all of the other groups of dogs were sampled, it is not possible to comment on any relationship of hair stage to season beyond stating that overall in the winter months there is a tendency for the anagen proportion to be greater than it is in the summer, but that, on average in these dogs as a whole, the anagen phase represents a small proportion of the total. Again, telogen predominated throughout the year except in December.

Of the 24 hypothyroid dogs, 11 had a high proportion of hairs in anagen (70% or more). These dogs were of the following breeds: Cairn (3), West Highland White (3), Yorkshire (2) and one each of the following, Lakeland, poodle and Pyrenean Mountain Dog. Ten dogs had a low proportion of hairs in anagen (30% or fewer). These were Labrador (3) and one each of boxer, chow, collie-x, Irish setter, Scottish terrier, Shetland collie and short-haired fox terrier. The Dachshund and Airedale fell into

a middle range, as did one poodle-x, which on one occasion had 36% and, on two other occasions, no hair in anagen in the samples examined.

Clearly, the effect of hypothyroidism was not sufficient to give any consistent difference in the anagen to telogen ratio as approximately equal numbers of dogs (11 : 10) were in each phase. Kristensen (1975b), examining a much smaller number of dogs (5) but by biopsy, also found no consistent effect of a thyroxine-responsive alopecia on the state of the hair follicles. There is, however, a suggestion of a relationship of breed to phase, in the results, but the numbers involved are too small for firm conclusions to be drawn.

From a consideration of the results of all groups, temporarily excluding Group One (Normal Dogs, A), it becomes evident that, where more than 3 dogs of a breed have been examined, there is a noticeable relationship between breed and predominance of anagen or telogen. This is seen in the Labrador and Labrador-x, of which 10 were examined on 13 occasions and all had over 96% telogen. Five boxers and boxer-x had between 98 - 100% telogen on 8 counts. Four collies, 3 collie-x and 1 Shetland collie (8 dogs) were examined 11 times with results of from 73 - 100% telogen (average 95%). Another composite group with a high telogen percentage consisted of 8 dogs described as terriers. They were of mixed breed and telogen ranged from 54 - 100% (average 85%). On the other hand, 9 West Highland White Terriers had anagen predominating with a range of from 70 - 100% and an average of 86% on 11

examinations. In 6 Cairn Terriers, the range was from 70 - 100% in 5 of the dogs (average 79% on 6 occasions) and 1 had 52% anagen on a single examination.

Of the remaining 34 dogs of 26 breeds, 25 were in telogen, 8 in anagen and one had approximately equal proportions of both kinds of hair.

Group One, normal dogs (A), contained 2 Labradors, 2 collies and 1 Cairn Terrier and each of these dogs fitted the pattern referred to above. The relationship of breed to predominance of either anagen or telogen is supported by the observation of Al-Bagdadi et al. (1977) that in their beagles, the anagen phase invariably predominated, irrespective of the dogs' ages or the season of the year.

No abnormalities were seen in the roots of hairs plucked from animals with skin diseases, whether hormonal or otherwise, or whether the hairs were in anagen or telogen.

Conclusions

1. In the dogs examined there was, overall, a predominance of telogen hairs.

2. The effect of breed was greater than the effect of disease, on the predominance of telogen or anagen phases of the hair growth cycle.

3. Hypothyroidism had no detectable effect on these phases.

4. The proportion of anagen hairs was greater in the winter than in the summer months, i.e. a single anagen peak occurred annually, in the dogs sampled monthly.

5. None of the disease conditions present affected the health of the roots of hairs which were plucked from the skin.

Suggestions for Further Work

Further study is required to elucidate the pattern of hair growth in different breeds and in dogs of different age and sex. Further information is also required about the effect of time of year on the proportion of the two phases. However, it is already evident that such studies are unlikely to add to knowledge regarding the diagnosis of specific diseases.

PROTEIN BOUND IODINE AND TOTAL IODINE VALUES IN SERUM

Until about a decade ago, it was considered that the assay of PBI was both reliable and significant in measuring canine thyroid function (e.g. from Meier and Clark, 1958, to Michaelson, 1969) but even during that period others had stated that the low PBI concentrations in the dog limited its diagnostic value (e.g. Kaneko et al., 1959, to Ekman et al., 1968). It was realised that the high level of serum inorganic iodine caused considerable error (Siegel and Belshaw, 1968). Also, PBI values, even when low, frequently remained within the normal range in apparently hypothyroid dogs and the test was thus unreliable as an indicator of thyroid function (Hightower and Miller, 1969). Capen at al. (1975) considered that PBI was not related to thyroid function but to iodine intake.

Many factors affecting PBI concentrations were discussed in the review of the literature. The effects of diet are clearly important. Farran and Bush (1971) fed proprietary food from which the iodine-containing dye tyrosine had been removed. Bush (1972b) ascribed the differences between his results and those of others to the differences in iodine content of different diets. Baker (1971) recommended that a low-iodine diet should be fed before blood samples were taken for assay.

The dogs which were blood sampled for PBI determination in the present investigation were on various

proprietary diets and household scraps.

In respect of one group of 6 proprietary dog foods, Anderson (1976) wrote that for product 1, the total iodine content was 4.0 ppm, for product 2 it was 5.9, 11.6 and 26.8 ppm in different samples taken within the course of 10 months, for product 3 it was 12.7 and 13.7 ppm on different occasions, for product 4 it was 15.2 ppm, for product 5 it was 4.0 ppm one year and 1.0 ppm the next, and for product 6 it was 2.0 ppm in one year and 1.1 ppm four years later. These levels refer only to samples taken on a particular day of manufacture and they indicate how great the possible fluctuation may be from one batch to another. Products 5 and 6 did not contain tyrosine but the other four did.

These communications, and the wide range of PBI values obtained and the lack of significant differences between the groups of dogs in the present investigation in respect of these values, made it clear that it was unprofitable to continue with this line of study.

SERUM CHOLESTEROL VALUES

In Group N, the mean and standard deviations for the cholesterol values, at the first assay, were 5.25 ± 1.85 mmol/l. Of the 68 results, 49 (72%) were within 3.4 - 7.1 mmol/l, i.e. mean ± 1SD and 8 dogs had lower and 11 dogs had higher levels (28%). These are the approximate groupings to be expected in the case of a normal distribution.

The mean + 2SD is frequently adopted in veterinary work to define the normal range of biochemical parameters. In the Group N dogs, this was 5.25 ± 3.37 mmol/l (mean ± 2SD) equal to 1.55 to 8.95 mmol/l at the first examination. No Group N dog had a value below this, the lowest being 1.59 mmol/l. However, 3 dogs, N40, N41 and N44 had values above 8.95 mmol/l, of 9.34, 10.93 and 9.67 mmol/l respectively.

The upper limit, when the mean plus 1SD is considered, i.e. 7.1 mmol/l, is comparable with the 7.12 mmol/l (275 mg/100 ml) reported by Munson and Belshaw (1966-67) as being the level above which hypothyroidism was indicated. A fasting value of 7.77 mmol/l (300 mg/100 ml) was suggested by Capen, Belshaw and Martin (1975) as being the level above which about two-thirds of hypothyroid cases would occur. The upper level associated with the mean plus 2SD, i.e. 8.95 mmol/l, is not as high as the 12.95 mmol/l (500mg/100 ml) above which McCullagh (1978) suggested hypothyroidism

should always be suspected in dogs. Otherwise, these workers, like others, while indicating that the levels they suggested were about the upper level for normal dogs, acknowledged that a proportion of hypothyroid dogs would also have cholesterol levels below these levels. For purposes of comparison with the results of the present investigation, the values in mg/100 ml, given by the authors quoted, have been converted to SI units, i.e. mmol/l.

The great variety of upper limits reported by others as occurring in apparently normal dogs, ranging from 3.89 mmol/l (150 mg/100 ml) (Kallfelz, 1973) to 25.20 mmol/l (973 mg/100 ml) in household pets (Schiller et al., 1964), makes meaningful comparison with the present results difficult. It lends support to the generally held view that the inter-laboratory comparison of results may not mean a great deal unless the methods used are identical and inter-laboratory quality control is adopted.

Most of the other workers cited in the review of the literature have given the upper level of the normal range as from 6.48 to 12.48 mmol/l (250 to 480 mg/100 ml) with a predominance of about 7.77 mmol/l (300 mg/100 ml). This level and the 7.1 mmol/l recorded here as the mean plus 1SD of cholesterol values obtained at the first examination of the normal dogs suggest that values greater than 8 mmol/l could reasonably be regarded as being above the normal range.

In 5 experiments, normal dogs were blood sampled at different intervals from immediately after feeding to 24

hours later. The longer post-prandial intervals to sampling included 19 hours on 5 occasions in 4 experiments, 21 hours twice, 22 hours once and 24 hours twice. No significant differences were found between the cholesterol levels at different post-prandial intervals within each group of dogs, i.e. it did not appear that the time of sampling in relation to the last feed affected the cholesterol levels. This is an interesting observation as it has been recommended that samples for cholesterol assay should be taken after a fasting period of 12 to 18 hours (Munson and Belshaw, 1966-67; Mason and Wilkinson, 1973). The reason put forward for this was to minimise the effect of the recent ingestion of food on the serum cholesterol levels. Lorenz and Cornelius (1976) also considered that the time of feeding influenced the cholesterol level. It does not appear, however, to have been unequivocally demonstrated that, in dogs, the effect of a recent feed is to raise the serum cholesterol level although the nature of the diet does affect the levels, as was shown in comparisons of pet dogs and kennelled dogs reported by Hoe and Harvey (1961) and Schiller et al. (1964). The pet dogs had the higher levels. To some extent this is also seen when the results of the first samples taken from Group N are compared with those taken when some of the dogs were hospitalised to study the effect of time of feeding on cholesterol values. The range of first cholesterol values was 1.59 - 10.93 mmol/l whereas during the experiments it

was 1.59 - 8.96 m mol/l. At the time of the first assay, many of the normal dogs, like those of the pet dog groups of Hoe and Harvey (1961) and Schiller et al. (1964) as well as receiving proprietary dog foods, were being given table scraps and titbits of various kinds. During the present experiments, however, their diet was standardised and thus lacked the human dietary supplements. The tendency, in the absence of household scraps, was for fewer dogs to have serum cholesterol levels at the upper end of the range.

The dogs of Group HS include those that had not been previously treated (HSU) and those that had (HST) at the time of first examination by the writer, although some of the HST Group had not been treated for some time. At first, the values for the HSU group were 8.51 $\pm$ 2.44 mmol/l, 22 of the 35 cases having first values over 8 mmol/l, with a maximum of 14.01 mmol/l. Not all of these dogs were available for a series of further cholesterol assays but results are available for 15 which were sampled more than once after treatment had started. In a total of 143 cholesterol assays, made during the course of thyroid therapy, 117 showed a reduction and 26 either no reduction or an increase in value from the first value of the case on which they were made. That is 81% of the results were lower than at first. Likewise results were available for 10 of the HSU cases that had cholesterol levels below 8 m mol/l at the first examination. In 62 assays made during

the period of treatment, 48 were lower and 14 were the same or higher than at first. That is 77% were lower. Overall, 80% of 205 assays of cholesterol during therapy were lower than the pre-treated assay and only 20% were not. An inspection of the results for each dog shows a variety of patterns, but the general tendency is for the cholesterol level to decline. Some, at least, of the fluctuations were due to the owners temporarily stopping treatment, when the tendency was for the values to rise again.

For six of the HST group for which more than 1 result was available after the resumption of treatment (by the writer), in 51 results, 31 were lower and 20 the same as or higher than the first assay. Here again, there was an overall reduction in 60% of the values. The proportion of reduced values is not as great as in the case of the HSU group but some of the HST group were already being treated when first seen by the writer.

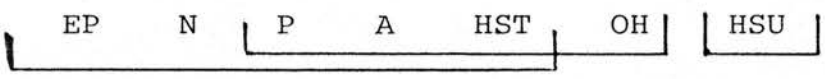
The reduction in cholesterol values is in keeping with the observations of Meier and Clark (1958), Mallo (1966), Ekman et al. (1968), Kaneko (1970), Rijnberk (1971), McCullagh (1978) and Bush (1979), who have referred to monitoring the effect of treatment by estimating serum cholesterol.

Despite the overall reduction in cholesterol levels associated with thyroid therapy, the values in some dogs remained near the upper part of the normal range (i.e. close to the 8 mmol/l (arbitrarily selected here) or went

above it. That is, the reduction in cholesterol values did not always parallel the clinical improvement, an observation similar to that of Belshaw (1971), and that of Rogers et al. (1975) who noted a mild hypercholesterolaemia in some treated dogs. Generally, the clinical improvements attributable to treatment preceded the reduction in cholesterol values.

Cholesterol values above 8 mmol/l were also found in the first samples of 5 dogs of Group OH, 7 of Group P, and 4 in both Group A and EP.

When the results of the first assays in all groups were subjected to an analysis of variance (Table 122), there was a very significant variance ratio ($P < 0.01$). When Duncan's new multiple range test was then applied, the subsets showed the following relationships in respect of cholesterol values.



The cholesterol values of the previously untreated cases of suspected hypothyroidism were significantly higher than those of all the other groups, including the previously treated cases of suspected hypothyroidism. Although the normal dogs and cases of external parasitism differed significantly from the 'other hormonal' group, none of these three groups differed significantly from the P, A and HST groups. This is also shown in Table 123 in which the proportions of dogs with elevated cholesterol levels (greater than 8 mmol/l) in each group are compared using

the Chi-square test. In this case both HSU and HST dogs have been considered as one group (HS). Here, the difference between the cholesterol levels of the group HS are seen to differ very significantly from those of the other groups.

The distribution of cholesterol values is illustrated in Figure 9 .

Table 122

Analysis of variance of cholesterol values in different groups of dogs

Group	Number of observations	Serum cholesterol mean ± SD mmol/l
N	68	5.25 ± 1.85
HSU	35	8.51 ± 2.44
HST	12	6.51 ± 2.99
OH	47	6.11 ± 2.05
P	85	5.61 ± 2.03
A	55	5.82 ± 1.56
EP	43	5.10 ± 1.77

Variance ratio 13.05 **

** $P < 0.010$

Table 123

Proportions of dogs in the different groups with serum cholesterol values (ECV) elevated above 8 mmol/l

Group	Dogs no.	ECV no.	Percentage
N	68	4	5.90
HS	47	23	48.9
OH	47	5	10.60
P	85	7	8.20
A	59	4	6.80
EP	49	4	8.20

	Degree of freedom	Chi-square
a All Groups	5	65.030 ***
Omit HS	4	0.980
b N	1	31.440 ***
HS		

P *** < 0.001

SERUM THYROXINE VALUES

Group N, Normal Dogs

The serum T4RIA values obtained in each of the 5 experiments showed no significant differences irrespective of the interval post-prandially that the blood sample was taken. It would thus appear that on ordinary diets, blood samples may be taken for T4RIA without regard to the interval since the previous meal. Since the samples were taken at different times of day i.e. from 9 a.m. to 5 p.m., it also appears that the time of day does not affect the values.

The values obtained in the experiments and the values obtained for other dogs of this group can be conveniently considered on the basis of either the T4 value of the first sample for each dog or of the mean T4 value where more than 1 sample was assayed. In the latter case, when the mean of multiple samples and the single result when only one was available, were used. The mean value of the mean values is 2.20 mcg/100ml $\pm$ 1.06, i.e. the SD of the mean of the means with a range of 0.87 - 4.7 mcg/100ml. Of the results from 65 dogs, considered on this basis, 51 (78.46%) were within the range of mean $\pm$ 1 SD, i.e. 1.14 - 3.26 mcg/100ml, and 9 (13.8%)were below and 5 (7.69%) were above it. No value was below the mean less 2SD and 1 dog had a value above the mean plus 2SD. These data indicate the likelihood of there being a normal distribution of values in the group with the expected range for normal dogs being from 1.14 -3.26 mcg/100ml in over two-thirds of cases. The lowest single

value recorded was 0.6 mcg/100ml. These results may now be compared with those of other workers who have reported on T4RIA. The lower end of the normal range has been considered to be 0.5 mcg/100ml (Blake and Lipinski, 1980), 0.7 mcg/100ml, (Reap et al., 1978), between 1.0 and less than 1.5 mcg/100ml (Kaneko et al., 1975; Kraft, 1975; Lorenz and Cornelius, 1976; Chastain, 1978; Martin and Capen, 1979). The lower end of the normal range was considered to be 1.5 mcg/100ml by Sims et al., (1977) and Ihrke (1979). Belshaw and Rijnberk (1979) put the lower limit at 1.52 mcg/100ml. Others have presented results which because of the circumstances cannot be regarded as defining the usual range, e.g. Premachandra and Lang (1977) recorded 0.2 mcg/100ml in dogs but did not state whether they consider this to be normal.

If the 65 dogs of Group N are considered in the light of the observations of others, inspection of the single assay results or of the mean for each dog shows that there were nil (0%) 10 (15.4%) and 8 (12.3%) dogs with values of less than 0.5, less than 1.0 and between 1.0 to less than 1.5 mcg/100ml respectively. That is, 18 dogs (27.7%) had values below 1.5 mcg/100ml. None of these dogs showed clinical signs.

Ihrke (1979) considers that values between 1.5 and 2.2 mcg/100ml are in a 'gray zone' i.e. that such values do not clearly define the dog's thyroid status.

Group HS, Dogs with Suspected Hypothyroidism

This group was regarded as consisting of those previously

untreated for hypothyroidism (HSU) and those that had been treated (HST). The values for first samples were 0.2 - 6.5 mcg/100ml, 2.61±1.52 (mean and SD) for HSU dogs and 0.5 - 3.2 mcg/100ml, 1.78 ± 0.98 (mean and SD) for the HST dogs.

In the 34 members of the HSU group, the numbers (and percentages) of dogs with first T4RIA values less than 0.5, 0.5 to less than 1.0, and 1.0 to less than 1.5 mcg/100ml were 1 (2.9%), 5 (14.7%) and 3 (8.8%) respectively, a total of 9 (26.4%).

Of the 12 HST group, the numbers (and percentages) of dogs with first T4RIA values within these levels were nil (0%), 4 (33.3%) and 1 (8.3%). The equivalent percentages for the dogs of Group N were 0%, 15.4% and (12.3%) respectively with a total of 27.7%.

All Groups of Dogs

When the results of first assays for T4 were compared, statistically, for the groups N, HSU, HST, OH, P, A and EP, the analysis of variance showed that there were some significant differences, $P < 0.05 > 0.01$ (see Table 124). Using Duncan's new multiple range test, the subsets are as follows.

P	EP	HST	OH	A	N	HSU

This shows that while the T4 values of Group HSU are significantly different from those of cases of pyoderma (P) and external parasitism (EP), they do not differ significantly from those of either the treated hypothyroid suspected cases,

Table 124

Analysis of variance of T4 values in the different groups of dogs

Group	No. of observations	Mean ± SD mcg/100ml (nmol/l)
N	65	2.19 ± 1.07
HSU	34	2.61 ± 1.52
HST	12	1.78 ± 0.98
OH	40	2.08 ± 1.42
P	73	1.75 ± 1.03
A	45	2.15 ± 1.37
EP	36	1.84 ± 1.28

Variance ratio 2.34*

*P <0.05 > 0.01

the 'other hormonal' cases, the dogs with allergic skin disorders or the normal dogs. These rather unexpected results require further consideration.

The possibilities requiring consideration include

a) the T4RIA was incorrectly conducted,

b) the, mainly, clinical criteria employed to categorise the dogs at first were wrongly chosen or were wrongly applied,

c) the T4RIA ranges used by others to categorise the different levels of thyroid status are too imprecise to use as standards.

Actual T4 levels by RIA reported by others from their cases of hypothyroidism are as follows.

Sims et al. (1977) had 2 cases with 0.47 $\pm$ 0.05 and 0.5 $\pm$ 0.01 mcg/100ml, respectively. Chastain (1978) reported, for 4 clinical cases and 1 non-clinical case, values of from 0.5 to 1.8 mcg/100ml (1.0 $\pm$ 0.48 mean and standard deviation), and noted that one of his clinical cases had a value of 1.8 mcg/100ml and that the non-clinical case had a value of 1.0 mcg/100ml. He referred to this dog as being 'apparently hypothyroid' or as having a 'subnormal baseline T4 value'. Reference has already been made to the results of Premachandra and Lang (1977) who reported 0.2 - 2.4 mcg/100ml (1.4 $\pm$ 0.69 mean and standard deviation) without indicating that the lower levels applied to clinical cases. Reap et al. (1978) reported 10 dogs, described as normal, as having a range of from 0.70 to 2.18 mcg/100ml

i.e. the lower results are in the range regarded as being subnormal. When the 'gray area' referred to by Ihrke (1979) i.e. 1.5 - 2.2 mcg/100ml is taken into account, doubt must be cast on the diagnostic value, except in the most general of terms, of the results of T4RIA. The impression to be derived from these relatively few reports is that the main basis for diagnosis continues to be the clinical findings, when a battery of tests is not undertaken. When the clinical picture is indicative of hypothyroidism and low thyroxine values are obtained, the diagnosis is regarded, apparently, as having been confirmed. If, in cases with signs indicative of hypothyroidism, the T4 values are above 1.0 mcg/100ml, up to about 1.5 mcg/100ml or even higher, the results appear not to be regarded as affecting the diagnosis and, as Ihrke (1979) states, these cases 'are handled according to clinical impression'. Frequently, he states, animals with only a mildly depressed T4 value respond dramatically to therapy.

The only useful, large-scale investigation with dependable results was that conducted by Belshaw and Rijnberk (1979) who investigated 126 normal dogs and 48 dogs in which primary hypothyroidism had been confirmed by a battery of independent methods. The scope of these independent investigations was such as to render the diagnosis unequivocal. Their T4RIA results clearly segregate the normal from the hypothyroid dogs and, from the figure illustrating their article, it would appear that all of the

hypothyroid dogs had T4RIA values lower than 1.0 mcg/100ml, whereas all of the euthyroid dogs, except one, had values above 1.0 mcg/100ml.

In the hands of the other workers cited here and in the present investigation, nothing like the same degree of segregation of hypothyroid cases from normal dogs was achieved by T4RIA. Clearly, the present writer and the others named have either to review their laboratory methods or review the clinical criteria which they employ. However, the latter does not appear to be the main problem as there is very good general agreement about the clinical signs which are to be regarded as important in hypothyroidism. Apart, then, from their acknowledged experience and skill in connection with canine hypothyroidism, how did Belshaw and Rijnberk (1979) achieve such clear cut segregation of the two groups of dogs?

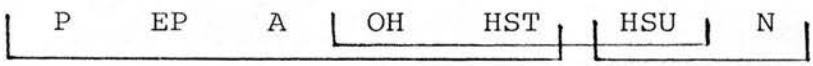
Simply, they did not use cases of suspected hypothyroidism as their basis. Instead, they used dogs in which the hypothyroid status had already been proved i.e. by definition they created the group for study. This means that by its very nature their investigation does not deal with the practical situation, as no information is given about the dogs which were not included but which must have been present in the preliminary selection process and which showed the usual signs of hypothyroidism. Indeed it would be from such animals that their group of hypothyroid (by laboratory definition) dogs was obtained. Their rejected cases would

be of the type which, because of negative results of laboratory tests for non-thyroidal disease, cannot be diagnosed as other than cases of hypothyroidism in the practical situation.

These thoughts are not intended as an adverse criticism of the valuable and interesting report by Belshaw and Rijnberk (1979) but they are to indicate that their results are only applicable in a carefully defined set of circumstances and that they do not alter the situation in respect of the so-called 'gray zone' of laboratory results, especially when the cases involved are clinically equivocal.

SERUM TRIIODOTHYRONINE VALUES

When the analysis of variance was made of the values of T3 of all the groups, the variance ratio was found to be statistically significant ($P < 0.01$), (see Table 125) indicating that there were significant differences between the groups. When Duncan's new multiple range test was applied the relationship of the subsets was as follows.



This revealed that the T3 levels of the HSU group were not significantly different from those of the other hormonal, the previously treated suspected hypothyroidism cases and the normal dogs, although they were significantly different from the values estimated for the pyoderma, allergy and external parasitism group of dogs. It is interesting that the normal group is significantly different from all of the other groups except the HSU group. The means of the HSU and N groups are higher than those of the other group.

From the review of the literature, the normal range of T3RIA is seen to be, in ascending order of the lower level, as follows.

0.20 - 2.06 ng/ml	(Kraft, 1975)
0.25 - 1.50 ng/ml	(Kallfelz, 1977)
0.42 - 0.87 ng/ml	(Premachandra & Lang, 1977)
0.48 - 1.54 ng/ml	(Belshaw & Rijnbeck, 1979)
0.60 - 2.00 ng/ml	(Martin & Capen, 1979)
0.63 - 1.30 ng/ml	(Reap et al., 1978)
0.75 - 1.00 ng/ml	(based on Capen et al., 1975)
0.75 - 2.00 ng/ml	(Sims et al., 1977)

In the present investigation, the lower limits of the

Table 125

Analysis of variance of T3 values in the different groups of dogs

Group	No. of observations	Mean + SD (nmol/l)
N	63	1.58 ± 0.77
HSU	30	1.49 ± 0.81
HST	12	1.04 ± 0.58
OH	46	1.19 ± 0.50
P	77	1.10 ± 0.57
A	48	1.15 ± 0.71
EP	36	1.14 ± 0.55

Variance ratio 4.67 **

** $P < 0.01$

T3 range of values for Groups N, HSU, HST and OH were at or above the lower limits of the ranges quoted above whereas the lower limits of the T3 values for Groups P, A and EP were considerably below.

No ready explanations are available for these findings, other than those discussed in connection with the T4 results. Again, apart from the clear-cut segregation of results reported by Belshaw and Rijnberk (1979), the results of others show considerable overlap in T3RIA values of hypothyroid and euthyroid dogs. For example, the data of Capen et al. (1975) suggest that most of their hypothyroid cases have T3 values of about 0.58 - 0.68 ng/ml whereas about half of the workers cited above regard those values as being in the normal range. Martin and Capen (1979) state that in hypothyroidism T3RIA is usually below 0.50 ng/100ml. Bush (1979) states that levels less than 0.50 ng/ml are found in hypothyroidism. On the other hand, Kraft (1975) found T3RIA to be as low as 0.20 ng/ml in normal dogs. Again, it would appear that, as for T4RIA, there is insufficient information about the results of T3RIA to use them as the sole factor in confirming the diagnosis of hypothyroidism even in dogs which appear to be clinically affected with the disease.

VALUES OF SOME SERUM ENZYMES AND OTHER BLOOD CONSTITUENTS

Although the differences between the mean values of SAP in Groups HS and N do not reach statistical significance, they indicate an interesting trend. The ranges of values for Group HS and Group N were 6 - 1120 IU/l and 6.4 -142 IU/l respectively, and in both cases the lower part of the range falls within the range regarded as normal by Hoe and O'Shea (1965), that is, 10-49 IU/l with values up to 284 IU/l for young dogs. Malherbe(1965) gives the range as 21-92 IU/l. In Group HS, the higher mean value (111.6 $\pm$ 169.65 IU/l, m$\pm$ SD) tends to suggest some degree of liver damage.

SAP values are also affected by skeletal disorders, but in the present context other hormonal disturbances such as diabetes mellitus and hyperadrenalcorticalism (canine Cushing's disease) may be more important. Both of these disorders are known to raise SAP values, because of their associated hepatotoxic effects. Blood and urine glucose levels and the response to insulin therapy help to distinguish diabetes mellitus from hypothyroidism. In Cushing's disease SAP values are elevated (Kelly and Darke, 1976) and the elevation of plasma cortisol levels also assists in the diagnosis, particularly when the response to the injection of adrenocorticotropic hormone is taken into account. In normal dogs this seldom doubles the plasma cortisol concentration but in cases

of Cushing's disease, there is a considerable increase following ACTH injection.

With a number of parameters, it is not always possible to compare the results of one laboratory with those of another. For example, with the fluorimetric equipment used in the present investigation, the normal range is 35 - 330 nmol/l (Doxey, 1978). The resting mean cortisol concentrations for all of the group in this study fell within that range and there was no statistically significant difference between the groups.

Others (Schalm, Jain and Carroll, 1975; Kaneko, 1979) have reported the normal range to be 24.8 - 153.3 nmol/l. Ling, Stabenfelt, Gribble and Schechter (1979) regard 342 nmol/l as the normal maximum value, which is rather similar to that accepted in the laboratory of the Department of Veterinary Medicine where the present work was undertaken. In 117 untreated cases of canine Cushing's syndrome, Ling et al. (1979) found the resting cortisol values to be 44.2 - 828.0 nmol/l (198.7 $\pm$ 129.7, m $\pm$ SD). Following ACTH stimulation, the value rose to a mean of 883.2 nmol/l, an increase of 1:4.44.

The following remarks apply either to dogs in the present study with cortisol values on at least one occasion greater than 331 nmol/l, the top of the normal range for this laboratory, or to dogs which because of their clinical condition, were considered to be cases of Cushing's disease. Not all of the dogs had their cortisol

concentration assayed.

In Group N, a clinically normal dog, N23, had a cortisol value of 624 nmol/l on one occasion. Unfortunately this was not followed up.

In Group HS, case HS7 was sampled on 7 occasions and on 3 of them the cortisol values were from 428 -483 nmol/l. When the ACTH stimulation test was done, the resting value was 165.6 and it rose to 772.8 nmol/l (1:4.67). This dog had a T4 value of 2.8 mcg/100ml and a cholesterol value of 11.20 mmol/l on first examination. Although the clinical signs were those of hypothyroidism, the results of the assays suggest the possibility of a combination of hormonal disturbance with adrenal dysfunction contributing.

Case HS8 had cortisol values of 331 and 384 nmol/l but these values were not considered high enough, in the light of the clinical findings, to warrant an ACTH stimulation test.

Case HS9 had cortisol assayed 5 times; 4 of the results were lower than 331 nmol/l but 1 was 552 nmol/l. Following the ACTH test on an occasion when the resting value of cortisol was 193 nmol/l, it rose to 496 nmol/l (1:2.57), an increase insufficient to suggest adrenal dysfunction.

Case HS14 had resting control readings of from 358 to 772 nmol/l. The relative increases on 2 occasions, following ACTH stimulation, were 1:1.4 and 1:1.85. These were not indicative of adrenal dysfunction. This dog had

a cholesterol concentration of 8.50 nmol/l, and T4 and T3 values of 2.20 mcg/100ml and 0.01 ng/ml respectively. Although the clinical signs suggested hypothyroidism, the T4 value was not low and the response to thyroid therapy was very slow. This dog may have had a combined endocrine dysfunction in which the clinical manifestation of hypothyroidism predominates.

Case HS31 had cortisol assays undertaken on 5 occasions, and on 2, the cortisol values were 358 and 611 nmol/l; the mean of 5 assays was 291 nmol/l. T4 and T3 values were low and the response to ACTH stimulation was not tested.

In these 5 cases of hypothyroidism, suspected on clinical grounds (Group HS), it is possible that 1 had a concurrent, but not clinically manifested, mild hyperadrenalcorticalism.

In Group OH, although case OH10 had cortisol values in the normal range on 3 occasions (330,220 and 55 nmol/l), the clinical findings and the result of skin biopsy were indicative of Cushing's disease. This was confirmed when the response to ACTH injection was 1:3.45 and 1:6.99 in 2 separate tests.

Case OH11 also had a low resting cortisol value (55 nmol/l). The clinical findings and the history of the case indicated iatrogenic Cushing's disease. Stimulation by ACTH raised the cortisol value 1:6.49, in confirmation.

Case OH12, clinically a case of Cushing's disease, had resting cortisol values of 441, 358 and 414 nmol/l

on 3 different occasions. ACTH stimulation, following the taking of the second and third samples, raised the cortisol values to 1600 nmol/l (1:4.47) and 2760 nmol/l (1:6.67), in confirmation.

Case OH13 had the clinical signs and history of iatrogenic Cushing's disease. The pre- and post-ACTH stimulation values of cortisol (nmol/l) were

330 to 1037 (1:3.14)
303 not done
386 to 993 (1:2.57) and at a late resampling this had risen to 1490 (1:3.86), supporting the clinical diagnosis.

Case OH25 had apparently adequate levels of T4 (2.30 mcg/100ml) and T3 (0.85 ng/ml) a cholesterol value of 4.06 mmol/l and clinical signs of alopecia and seborrhoea. The resting cortisol value was 1117.8 nmol/l. ACTH stimulation was not done in view of the high resting cortisol value which was taken to indicate the likelihood of adrenal cortex dysfunction leading to the dermatosis.

Case OH47 was on clinical grounds a case of Cushing's disease. The T4 and T3 values were 0.60 ng/100ml and 1.05 ng/ml respectively, the former being below the normal range referred to by others. Cholesterol concentration was 9.52 mmol/l. The resting cortisol values ranged from 27.6 to 469.2 nmol/l with a mean of 202.87 $\pm$ 140.6 SD for 12 separate occasions on which it was evaluated. ACTH stimulation tests were done on occasions when the resting cortisol values were 165.6, 96.6, 55.2, 27.6 and 55.2

nmol/l. The post-stimulation readings were 276, 607, 262, 27.6 and 193 respectively (1:1.66; 1:6.28; 1:4.75; 1:1 and 1:3.49). The magnitude of 3 of the responses supports the clinical diagnosis.

In Group P only 1 dog of those in which cortisol was assayed had values over 331 nmol/l. This was case P21 which had cortisol values of 386, 324 and 496 nmol/l and 2 lower values, on the 5 occasions. ACTH stimulation raised 324 to 622 nmol/l (1:1.92), a diagnostically insignificant response.

In each of Groups A and EP, one dog of those assessed for cortisol concentrations had a value of 331 nmol/l. None had high concentrations.

Thus, although the resting levels of cortisol were not significantly different between the groups, the results of the ACTH stimulation test were found to accord very well with the clinical diagnosis.

Assays were made of blood urea and blood glucose in a number of the dogs in each group but without a significant difference being demonstrated between the groups. The sporadic nature of the sampling renders further discussion of this aspect unprofitable.

Reference has already been made to the concentrations of serum alkaline phosphatase. There was no significant difference between the groups in respect of this enzyme but higher values were observed in the groups HS and OH than in Group N. Elevated SAP concentrations are

associated with liver damage, such as occurs in Cushing's disease. The mean SAP for Group N was 44.72 IU. Of the 6 dogs of the OH group referred to in this section, SAP was assayed on a number of occasions in 5. The highest SAP value obtained for each dog was 1940 IU/l for case OH10, 750 for OH11, 325 for OH12, 635 for OH13 and 2310 IU/l for OH47. That is, the possibility of liver damage being present was high in them all. For all dogs of Group OH in which SAP was assayed, the mean value was 411 IU/l i.e. approximately ten times greater than the mean SAP for Group N.

HAEMATOLOGICAL INVESTIGATIONS

In diagnosing anaemia the main parameters considered are the RBC numbers, Hb levels and PCV, with the indices MCV, MCH and MCHC. The means and standard deviations of the results had variance ratios that were statistically significant only for Hb ($P<0.05 >0.01$) and MCH ($P < 0.01$) (see Table 115). When these parameters were subjected to Duncan's new multiple range test, it was shown there was no single group of dogs with Hb statistically different from all the others; the significant subsets included 4 or 5 groups. The previously treated (HST) and untreated (HSU) hypothyroid suspected cases were in the same subset for Hb as the normal dogs and those with allergic skin conditions. In addition the HSU group and the group with external parasitism (EP) were not significantly different. The EP group was the only one from which the HST group was significantly different.

Regarding MCH, there was a clearer division, into two non-overlapping subsets. The smaller of these contained the HSU and EP groups only and they significantly differed from all of the other groups.

In a consideration of the individual members of each group, the number of dogs with anaemia was as follows, using as standard those referred to (Doxey, 1971) in the review of the literature.

Group N	0 cases in 49
Group HSU	3 cases in 34
Group HST	1 case in 11
Group OH	2 cases in 44
Group NH,P	4 cases in 80
Group NH,A	1 case in 54
Group NH,EP	2 cases in 35

From the analysis of the inter-group relationship and the numbers of affected dogs in each group, it is evident that haematological studies are of little help even in a supporting role in diagnosis, despite the views expressed that it is often present sub-clinically (e.g. Munson and Belshaw, 1966-67; Theran and Thornton, 1966; Bush, 1969a; Belshaw, 1971; Rijnberk, 1974) nor even rather consistently manifested (Hollander et al., 1967; Baker, 1971)or in most cases (Kaneko, 1970; Capen, Belshaw and Martin, 1975; Kallfelz, 1977;Martin and Capen, 1979). It is, however, correct that in the present study 10% of the suspected hypothyroid cases had mild, sub-clinical anaemia when its occurrence in the other groups was at less than half this level. The two cases in the EP group were affected with clinically evident, marked anaemia due to the severity of their burden of external parasites, and one later died from this cause. It does not appear to be advantageous to discuss the individual cases further.

THE RELATIONSHIP OF LOW CONCENTRATIONS OF T4 AND T3 TO CLINICAL FEATURES

THE RELATIONSHIP OF LOW CONCENTRATIONS OF T4 AND T3 TO CLINICAL FEATURES

An important part of this study has been the attempt to define hypothyroidism from a clinical viewpoint and of distinguishing it from a number of other conditions, also primarily on clinical grounds. Next, the laboratory features associated with the groups of diseases were categorised. The question remains as to whether it is possible to approach the problem from the viewpoint of the laboratory findings i.e. of low thyroid hormone values in a group of dogs, and then of reviewing the clinical signs that were present so that the clinical picture may be even more precisely defined.

Values usually regarded as being indicative of thyroid deficiency are below 1.5 mcg/100ml for T4 and below 0.5 ng/ml for T3. These values were applied to the individual dogs in all the groups. The results are shown in Table 126.

TABLE 126

The number and proportion of dogs at time of first examination with values of T4 and T3 below 1.5 mcg/100ml and 0.5 ng/ml respectively

Group	Dogs in Group	Dogs with T4 & T3 Values Stated	
		No.	%
N	62	1	1.61
HS	41	3	7.32
OH	40	1	2.5
P	73	5	6.85
A	45	2	4.44
EP	36	2	5.55
All	277	14	5.05

from which it is evident that even at the low level of values adopted, there are dogs in every group which apparently fulfil the biochemical requirements for hypothyroidism. A similar exercise using such standards as T4 and T3 values lower than 1.5 mcg/100ml and 1.0 ng/ml, respectively or below 1.0 mcg/100 ml and 1.0 ng/ml respectively makes little difference to the proportion of each group included but the actual number of dogs included is larger. At the lower combination, less than 1.0 mcg/100 ml of T4 and less than 0.5 ng/ml of T3, no normal dog is included but the proportions of the other groups remain much the same only the number involved is small i.e. a total of 11 dogs in 277. When T4 alone is considered at below 0.5 mcg/100ml only 6 dogs are included.

The clinical signs presented by the dogs having values of T4 less than 1.5 mcg/100ml and of T3 less than 0.5 ng/nl were as follows.

In Group N, 1 dog with no signs of clinical abnormality was included.

In Group HS, 3 dogs were included. HS13 was a male Airedale, 10 y.o. HS20 was a female Doberman, 11 y.o. and HS40 was a female Labrador 6 y.o.

Clinical Findings	Dog No. HS13	HS20	HS40
Alopecia	+	+	+
Lethargy	+	+	+
Inflamed skin	+	+	+
Weight gain	+		+

In addition, HS13 had comedones, otitis externa, thermophilia and polyphagia. HS20 had gynecomastia and weight loss, and HS40 had a sparse, dry coat.

In Group OH, only 1 dog, case number OH11, a male retriever, 8 y.o., was included. It had an inflamed, pruritic skin, was lethargic and had gained weight. Calcinosis cutis was identified on skin biopsy and Staph aureus on skin culture. The cholesterol concentration was 9.05 mmol/l. Injection of ACTH raised the cortisol concentration from its resting value of 55.2 nmol/l to 358.8 nmol/l (1:6.49). The dog had been subjected to corticosteroid therapy at intervals over the previous 3 years for suspected contact dermatitis. The history and clinical findings were indicative of iatrogenic Cushings syndrome and pyoderma.

In Group P, 5 dogs were included:

P9 Terrier, male, 9 y.o.
P10 Border collie, male, 1 3/12 y.o.
P14 Alsatian, male, 3 y.o.
P72 Labrador, female, 3 6/12 y.o.
P85 Pug, male, 8 y.o.

Their clinical features were as follows:

Dog. No.	P9	P10	P14	P72	P85
Clinical features					
Dermatitis:					
Acute	+	+	+	+	+
Mild	+	+	+	+	+
General					+
Local	+	+	+	+	
Pruritus	+	+	+	+	

These dogs were all affected with pyoderma. In addition P72 and P85 had areas of hyperpigmented skin. P85 also had hyperkeratosis and increased body weight.

In Group A, 2 dogs were included, A17 a female Old English Sheep Dog, 2 6/12 y.o. and A30, a female boxer 1 y.o. Both had seasonal dermatitis with pruritus. In A17 this was severe and localised whereas in A30 it was generalised but mild. A30 also had areas of thickened and hyperpigmented skin and of alopecia. Neither dog was overweight or lethargic and the alopecia in A30 was irregular.

In Group EP, 2 dogs, EP1 and EP22, were included. Both showed signs of chronic, severe generalised dermatitis with erythema, scaliness and pruritis. EP22 also had some thickening and hyperpigmentation of the skin.

Of these 14 dogs only 3 had signs of alopecia plus lethargy plus mild dermatitis, and 2 of them were overweight. All 3 were in Group HS. One other dog was lethargic and overweight but its history and clinical signs were indicative of iatrogenic Cushing's syndrome and pyoderma. None of the 5 dogs of Group P showed alopecia or lethargy but all had clinically evident pyoderma and no other noteworthy features. Neither of the dogs from Group A was lethargic or overweight but 1 had an area of alopecia together with other indications of an allergic disorder. Both dogs in Group EP were typical cases of external parasitism and neither was affected with lethargy, alopecia or overweight and the dermatitis was different

from the very mild form encountered in some typical hypothyroid cases.

Thus, the attempt to work from laboratory findings, using low values of T4 and T3 as the standard, has had no appreciable effect in re-defining the clinical features. The alternative, which has not been accepted by any worker, is that hypothyroidism is capable of simulating skin diseases of many kinds but without necessarily presenting any of the combinations of signs (symmetrical alopecia, lethargy, weight gain) that have been widely associated with the disease in the dog and man.

In this deliberate attempt to restrict the way in which the disease was considered, there were combinations of lethargy, alopecia, mild inflammation of the skin without pruritus, and overweight appearing rather consistently in and only in the dogs selected from Group HS, while the only sign common to the other dogs was dermatitis, often severe, associated with well-marked and even self-injurious pruritus. This is quite distinct from the picture presented by the dogs from the HS group.

It may be said that these examples, drawn from the larger groups on the basis of the low thyroid hormone levels alone, have less in the way of overlapping of signs than even the larger groups have.

Munson and Belshaw (1966-67) have stated that there are probably as many cases of sub-clinical hypothyroidism as there are of the overt variety. This refers to the

biochemical status of these cases i.e. they have low levels of circulating thyroid hormone but do not evince clinical signs. This view is amply supported by the findings in the present investigation when dogs with low levels of thyroid hormone not only showed the signs regarded as being typical of the disease but other dogs with similarly low values appeared in good, normal health and others again were affected with a variety of disorders, many of them distinguishable from hypothyroidism on clinical grounds or laboratory investigation. Here it may be said that although a discussion of the aetiology of all cases in the group described as being affected with other hormonal disorders (Group OH) has not been presented, detailed investigations of the kind outlined for case OH11 were conducted on them also. These included biopsy of skin and testicles, bacteriological culture, the assay of thyroid hormones, cholesterol and cortisol, and the use of the ACTH stimulation test where such seemed appropriate. That is, cases which could resemble hypothyroidism were usually distinguished by the use of other tests.

It is a matter for speculation whether a sub-clinical reduction of skin health associated with low levels of thyroid hormone in dogs which are not showing signs of deficiency, predisposes to pyoderma. The present investigation does not elucidate this matter but Anderson (1974) considered that endocrine disturbance predisposed to seborrhoea which affords a good medium for microorganisms and secondary infection is regarded as a fairly frequent

complication in hypothyroidism (Bush, 1969a; Ihrke, 1979).

This thesis has not been concerned with the effect of thyroid replacement therapy on the clinical cases. Cases were treated by the usual methods but it is not intended to discuss them here. It is of interest, however, that 3 dogs of Group HS, namely HS1, HS32 and HS36 which on clinical grounds were suspected to be cases of hypothyroidism, recovered spontaneously. Findings in these 3 cases were as follows.

Finding	Dog No:	HS1	HS32	HS36
T4 mcg/100ml		0.55	1.25	6.4
T3 ng/ml		0.80	1.25	2.0
Cholesterol mmol/l		8.21	4.06	11.9
Skin inflamed		+	-	-
Alopecia		symmetrical	asymmetrical	asymmetrical
Lethargy		+	+	+
Weight gain		+	+	-
Dry sparse coat		-	-	+

On the usual clinical and laboratory criteria HS1 would be regarded as most probably a case of hypothyroidism although some may regard the T3 value as slightly high for this. However the low T4 and high cholesterol values would tend to counterbalance this opinion. Case HS36 has high values for both T4 and T3. There is no simple way of accounting for the spontaneous recovery of at least case HS1. However, the British Veterinary Association (1961) states that some cases recovered spontaneously and Mallo (1966) considered that therapy could sometimes be discontinued entirely. This is not the generally held opinion. Whatever the reason may be for the spontaneous recovery in these cases, there is little doubt that if these dogs

had been undergoing treatment, their improvement would have been ascribed to that. This casts doubt on the value of diagnosis by therapy which has been referred to as a possibility for consideration when other diagnostic methods have failed or are not available (Parris & Parris, 1966; Munson & Belshaw, 1966-67; Rijnberk, 1971; Bush, 1972a; Belshaw & Rijnberk, 1975b). Furthermore, there is a dispute as to whether the administration of thyroid or the synthetic preparations with the same effect is beneficial in cases of dermatosis or alopecia of non-thyroidal origin. Bornfors (1958) and Schwartzman (1966) stated that acanthosis nigricans responded to such treatment but this was not the experience of Bush (1972c). Kirk (1979) states that acanthosis nigricans is rare in hypothyroidism. Encouraging results from thyroid therapy in various dermatoses and cases of alopecia have been reported by Wright and Hoover (1961), Kristensen (1975b) and Bagnall (1977). If low concentrations of thyroid hormones are fairly commonplace in cases with a variety of skin disorders, as the present work has shown, and if, as may be the case, these low concentrations predispose some dogs to other skin conditions such as pyoderma, it must remain an open question at present as to whether thyroid therapy in such cases may not confer benefit. This would be on the basis of the generally beneficial effect that thyroid hormone has on the skin and coat, one of the effects normally ascribed to it.

GENERAL DISCUSSION AND CONCLUSIONS

GENERAL DISCUSSION AND CONCLUSIONS

Dogs were primarily selected from the intake to the Clinic or Hospital on the basis of their having some abnormality of the skin or coat or because they represented some other clinical sign e.g. feminisation, that distinguished them, even superficially, from other dogs, as being cases of dermatoses or possible endocrine dysfunction. A total of 299 such dogs was selected for more thorough clinical examination. On the basis of the facts derived from detailed history taking and complete physical examination, repeated as necessary, it was possible to partition these dogs into separate groups.

The groups consisted of dogs with suspected hypothyroidism (Group HS), those suspected of having other hormonal disorders (Group OH) and those with non-hormonal skin disorders such as pyoderma (Group P), allergic dermatitis (Group A) and external parasitism (Group EP). A separate group of 68 clinically normal dogs was employed for purposes of comparison.

Retrospectively, the adequacy of the clinical partitioning was supported by statistically significant difference in the incidence of certain of the clinical findings and/or by the difference in quality or character of the clinical signs that were common to many of the dogs.

Important clinical findings were alopecia, lethargy and body weight increased above the normal. Their incidence was significantly greater in Group HS than in

Group OH, the other group in which cases were most likely to be suspected of hypothyroidism on clinical grounds. Dermatitis was also a frequent finding but whereas the factors mentioned above differed in a numerical manner between the groups, dermatitis varied very much in its nature. In Group HS its character was typically mild and either non-pruritic or only slightly so, whereas in the other group with the exception of Group OH, it was often severe and intensely pruritic.

When combinations of the 3 clinical factors that are significantly different in Groups HS and OH were considered, the differences between the two groups were striking. In Groups HS and OH, respectively, alopecia plus lethargy plus overweight occurred together in 55.3% and 2.1% of dogs, alopecia plus lethargy occurred in 68.1% and 2.1%, alopecia plus overweight occurred in 67.0% and 12.8% and lethargy and overweight occurred in 63.8% and 8.5%. That is, in dogs suspected of having thyroid or other hormonal dysfunction, the combination of 2 or 3 of these factors is very important in clinical differential diagnosos. The occurrence of these combinations in non-hormonal diseases is extremely uncommon.

It appears that the increase in weight above the normal that occurs in hypothyroidism is less a matter of increased appetite but of the retention of normal appetite together with the physical sluggishness that is indicative of depressed metabolism.

One of the problems of comparing the present findings with those of others in that most of the other reports do not relate the incidence of aspects of hypothyroidism to any standard such as that of a local population or even a clinic population. The present study used two different external standards, namely all the dogs, 7,802 and the 686 cases of dermatoses, passing through the Clinic during a 3 year period. These 2 groups are referred to as the Clinic population and the selected population respectively. Both larger and smaller breeds of dogs were equally represented in Group HS but in comparing them with the selected population the ratio of large dogs affected was 1: 16.6 and for small dogs it was 1:12.8. This suggested that, despite previously expressed views to the contrary, the true incidence may not be greater in the larger breeds. On the basis of the expected incidence in the larger breeds, Labradors had a high incidence whereas collies, spaniels and Alsatians had a low incidence. In the small breeds, a higher than expected incidence was found in dachshunds, and 3 terrier breeds, the Cairn, Scottish or West Highland White. The numbers of dogs in the other breeds present were sometimes rather small to draw firm conclusions but the impression was gained that, in comparison with the selected population, the Chow Chow, Doberman, Lakeland terrier and Yorkshire terrier were overrepresented and thus apparently more susceptible, and that terriers of other breeds or mixed breeding

were underrepresented and thus much less susceptible to hypothyroidism.

Group HS dogs ranged in age from 10 weeks to 13 years and if the 2 youngest are excluded, the mean was 7.4 years, with the ratio of younger to older dogs being 18:29 taking 7 years of age as the turning point. The age at the time of first examination was 7.7 years and 6.7 years for males and females respectively but the latter showed 2 peaks of frequency at 2-3 and 7-9 years of age, unlike the male dogs. It may be that the occurrence in the younger of the females represents a period of greater sexual activity with the possibility of other hormonal disturbances, than in later life. This possible relationship remains to be investigated.

There was a relationship between the age of onset of the disease and the size of the breed, larger dogs showing first signs at 5.8 years and smaller dogs at 8.0 years. This may account, in part, for the opinion that the larger breeds are more prone to the disease. If it is accepted that some of the signs of hypothyroidism resemble those of ageing, e.g. lethargy, overweight and poor coat, then the natural ageing processes in the smaller dogs may sometimes obscure the development of these signs. The ageing processes are less likely to have this effect at 5.8 than at 8 years of age.

It has been customary, with the exception of a few authors, to state that the incidence of the disease is

equal in male and female dogs. The present findings cast doubt on this also. In Group HS, the male:female ratio was 1:2. In the Clinic population it was 1:0.8, a statistically significant difference between the group and the population. That is, the incidence in females is some two and a half times greater than in males than would be expected from the proportions in the Clinic population. This was significant at the $P < 0.01 > 0.001$ level.

It also appears, on the same basis, although the numbers involved are small, that castrated males and spayed females are at greater risk than the entire animals to which reference has just been made.

Even in an internal comparison, the proportion of females to males is highly significantly different in Group HS from the other groups studied.

A clinically detectable thickening of the skin was present in 21.3% of Group HS, a fact frequently mentioned by others. This matter was subjected to a separate investigation, in which skin thickness was measured with callipers at 15 different sites on 84 dogs from the various groups. Only one site, the groin, was found to be significantly thicker in Group HS (and Group OH) than in the other groups. This was not a breed effect. Thus no reliance can be placed on objective skin fold measurements to segregate hypothyroid cases from other dogs. This does not detract from the fact that clinically

evident thickening of the skin does occur in hypothyroidism.

The disorders of hair growth in hypothyroidism, clinically shown by such characteristics as alopecia and sparseness, dryness and roughness of the coat in some cases, was investigated by studying the stage of hair growth in dogs from the different groups throughout a year. There was a predominance of the telogen stage in all groups, although the proportion of anagen hairs tended to be greater in winter than summer. There was no difference between the groups that could not be related to the effect of breed. Breed type and not hypothyroidism decided whether telogen or anagen phases would predominate, in the present observations.

When serum cholesterol was assayed at various intervals pre- and post-prandially in normal dogs fed on commercial dog foods once daily, no significant differences were found. This finding brings into question the necessity of obtaining fasting blood samples except when the diet contains much in the way of household scraps. The present results support the findings of others that such a diet results in higher serum cholesterol levels than does a proprietary diet. The time of day at which the samples were taken for assay also did not affect the results.

In the larger investigation on the groups, serum cholesterol levels were significantly higher in previously untreated members of Group HS than in any other group.

When the cholesterol values of dogs undergoing thyroid therapy were estimated, 80% of 205 assays revealed a reduction in value for the pre-treated levels. There was, however, a variety of patterns observed in the individual dogs. Although the general tendency was for cholesterol values to decline, some dogs had values that remained near or above the upper part of the normal range, i.e. 8 mmol/l. The reduction in level did not always parallel the clinical improvement.

T4 was assayed at different times pre- and post-prandially in normal dogs but no significant differences were found either in relation to the time of feeding or the time of day. In the larger investigation into the groups, T4 values in 65 normal dogs ranged from 0.87 - 4.7 mcg/100ml (2.20 $\pm$ 1.06, m $\pm$ SD). 78.46% of these dogs had values within the range of the mean $\pm$ one SD with 13.8% below and 7.69% above these values. If the conventional 1.5 mcg/100ml is taken as the lower limit of the normal range, 18(27.7%) of the 65 dogs had a biochemical hypothyroid status but all were clinically normal.

Statistically, the T4 values of untreated members of Group HS were significantly different from those of Groups P and EP but not from those of previously treated HS dogs or the members of Groups OH, A and N.

Although the T3 values of the untreated HS dogs were not significantly different from those of the previously treated HS dogs and dogs of Groups OH and N, they did

differ significantly from those of Groups, P, A and EP.

The estimation of protein bound iodine was of no value, a fact that merely confirmed current opinion.

Haematological investigations added little although 10% of Group HS had mild subclinical anaemia and in the other groups it occurred with less than half this frequency.

The presence of liver damage in hypothyroidism and some other disorders led to the estimation of serum alkaline phosphatase and other enzymes. It was evident that although statistical significance was not reached between the results, both the HS group and the OH group had raised levels of SAP. Of greater interest were the levels of circulating cortisol, especially when the ACTH stimulation test was applied. This was particularly useful in adding to the writer's knowledge about dogs affected by Cushing's disease or iatrogenic Cushing's disease, as these cases showed the typical much increased cortisol levels post-stimulation whereas this was not the case in the other group. There was an indication, however, that sub-clinical Cushing's disease might occur concurrently with hypothyroidism.

The results showed that both healthy dogs and those affected with a variety of syndromes could have thyroid hormone levels that extended from well below the usually accepted normal range up into the normal range. That is, no diagnosis can be based simply on the fact that a dog has a low level of T4 or T3. Such dogs can only be

described as being in a state of biochemical hypothyroidism. The fact that dogs with e.g. specifically diagnosed Sertoli cell tumour, Cushing's disease and external parasitism may also have very low thyroid hormone levels further complicates the situation and increases the risk of misdiagnosis unless meticulous history taking and physical examination are undertaken together with the use of such laboratory methods as are known to be specific for these disorders.

The occurrence of biochemical hypothyroidism in dogs with pyoderma indicates the necessity for further investigations into the effect of low levels of circulating thyroid hormone on skin health in cases which do not show the classical signs of hypothyroidism.

Conversely, of course, the presence in apparently hypothyrotic dogs, showing no sign of other disease and not positive to the laboratory tests for other diseases, of T4 and T3 values in the normal ranges, also creates difficulty. The spontaneous recovery of some apparently hypothyrotic dogs casts doubt on the usefulness of employing therapy as a diagnostic procedure.

It is of interest that, when the enquiry was from the viewpoint of adopting the conventional biochemical standards for hypothyroidism, and applying these to the clinical findings in the dogs of all groups, the result was to confirm the opinion reached previously. That is, that hypothyroidism is primarily to be diagnosed on the

basis of clinical findings and that the forms of T4 and T3 tests used in the present study promote results that may merely support the diagnosis but cannot refute it.

In the history of the development of laboratory methods for the specific diagnosis of hypothyroidism, each new procedure has been greeted with enthusiasm, but few appear to be of real value in the day-to-day work of veterinary practice except that of ascertaining the response to injection of thyroid stimulating hormone. In retrospect, it is to be regretted that the decision to omit this test in the present study, in an attempt to segregate the groups solely on the basis of the levels of T4 and T3 in unstimulated dogs, was adhered to.

The enzyme linked immunosorbent assay (ELISA) for determining circulating thyroxine values in dogs appears to offer some promise. Larsson and Lumsden (1980) concluded that it was an acceptable alternative for use in laboratories lacking equipment for measuring radioactivity but stated that it was imprecise at low T4 levels. However, they note that if the absolute T4 values are ignored and the results of ELISA pre- and post the administration, of TSH are accepted, there is a good separation of the euthyroid from the hypothyroid dogs. Another alternative that also merits further investigation is that introduced, as yet unsuccessfully in the dog, by Chastain (1978) of assaying the concentration of circulating thyroid stimulating hormone.

IN RETROSPECT

IN RETROSPECT

In retrospect, a more critical assessment of the clinical basis of the allocation of the cases to the various groups, merits consideration. The original allocation was on the basis of the history and main presenting signs at the time of the first examination, supported by the preliminary laboratory tests referred to elsewhere.

It has already been shown statistically that there is a significant difference in T4 concentration between Group HS and Groups P and EP. Thus, it appears that on this basis, there is no need to review Groups P and EP, i.e. the clinical criteria were adequate. There is no significant difference in the T4 values between Groups HS and Groups OH, A and N, but there is no clinical criterion that would have enabled Group N dogs, which were clinically normal, to be reassigned. The dogs assigned to Group A were affected with allergic dermatoses and the syndrome was sufficiently distinct from those presented by the other cases to enable these dogs also to be assigned to their own group.

The groups which merit further consideration on purely clinical grounds are HS and OH. The picture is complicated by the fact that at least one of the HS cases later became a case of iatrogenic Cushing's disease and one of the OH group which was presented with the history

and signs of iatrogenic Cushing's disease in the first instance, had become so because it had been previously treated with corticosteroids, although an earlier diagnosis of the referring veterinarian was suspected hypothyroidism.

The reassignment on clinical grounds of members of Groups HS and OH would depend on the presence of some clinical feature, i.e. in the history or physical findings, that had been given insufficient weight previously. Furthermore, this problem would be mainly present in respect of the OH cases regarded as spontaneous or iatrogenic Cushing's disease or those assigned to the HS group, but which had dubious characteristics.

Important clinical features usually regarded as not present in hypothyroidism, but present in cases of Cushing's disease are polydipsia/polyuria, polyphagia, calcinosis cutis, abdominal enlargement (pot belly), and tenting of the skin when it is lifted followed by a slow return to its normal position. In the present research, an important question is whether some of the cases ascribed to Group HS were really cases of Cushing's disease. Thirteen of the 47 dogs in Group HS had at least one of the signs to which reference has been made. Of the 13 dogs, only four had more than one of these signs. These four dogs had polyuria/polydipsia plus polyphagia. The other nine dogs had only one of the signs, i.e. two had polyphagia alone, two were pot-bellied alone,

one had polyuria/polydipsia alone and one had tenting of the skin alone. None of them had calcinosis cutis. With the exception of two of the thirteen dogs showing one or more of the signs which could possibly have been ascribed to Cushing's disease, all had groups of signs indicative of hypothyroidism, i.e. all were lethargic, all had gained weight and all were affected with alopecia which was symmetrical in ten of the eleven cases. Eight of the eleven had mild dermatitis, another two had seborrhoea and three had thermophilia.

In summary, the weight of the evidence from the history and the physical findings was not strongly in support of these cases being other than hypothyroid. However, future research of this kind would benefit from being conducted on a much smaller scale so that fewer cases could be subjected to a larger range of laboratory investigations or, alternatively, that the in-depth investigations would be conducted over a much longer period of time. This would enable all suspected hypothyroid cases, in which there was even one sign which could be ascribed to Cushing's disease, to be investigated for the possibility of the presence of the latter disease. Likewise, in view of the fact that well-developed signs of Cushing's disease may obscure the possibility that a dog is also affected with hypothyroidism, it would be desirable to investigate the thyroid status of Cushing's disease cases. Furthermore, some cases of Cushing's disease have moderately to depressed plasma T4 and T3 concentrations. These cases should also undergo the TSH stimulation test.

In the present investigation, TSH stimulation tests were not undertaken because a primary aim was to attempt to distinguish cases of hypothyroidism on a combination of clinical grounds and serum T4 and T3 levels, from the other dogs in a large series. The investigation clearly demonstrated that dogs showing all the widely accepted clinical manifestations of hypothyroidism may or may not have T4 and T3 concentrations below the level generally regarded as normal. Furthermore, amongst both clinically normal dogs and dogs affected with a variety of disorders, there were instances of low thyroid hormone concentration. This has already been fully discussed, but the reiteration is necessary to define one of the objectives of the investigation, namely, to demonstrate the apparent absence of any real relationship between thyroid hormone levels in the dog and the clinical picture, making use of an ordinary clinic intake. Other investigations reported have been on a smaller scale; usually dogs showing signs other than of hypothyroidism were not included and often there were no clinically normal controls. Furthermore, it has been commonplace for most of the other workers to make statements to the effect that a particular case had a high normal baseline (i.e. when the clinical signs were of hypothyroidism but the hormone levels were in the normal range), or that the dog had an unusually low normal baseline (i.e. when the dog was clinically normal but had low thyroid hormone levels). Thus, such reports have not been particularly helpful in

establishing the true situation.

As has already been noted, the only publication that clearly differentiates between hypothyroidism and euthyroidism in the dog on the basis of T4 RIA levels, is that by Belshaw and Rijnberk (1979). In their investigation the result was to be anticipated as they selected dogs that, by other methods, were already known to be deficient in circulating T4 or to have normal levels, respectively.

Other workers have suggested that T4 RIA is inadequate as the sole test but none appears to have undertaken an experiment of sufficient scope to demonstrate the fact statistically.

However, despite these thoughts, it is desirable that the definitive diagnosis of hypothyroidism should be based on more than the clinical features. The response to thyroid replacement therapy has already been mentioned and it cannot be relied upon as a definitive diagnostic procedure. At prese then, the method employed in the clinical situation is to give a suspected case an injection of thyroid stimulating hormone and to estimate T4 and T3 levels before and at intervals after the injection as was discussed in the review of the literature. In euthyroid dogs, the effect of the injection is to raise the level of circulating T4 and T3 whereas in dogs with primary hypothyroidism, the increase is slight or absent. In secondary hypothyroidism, there is an increase which may almost approach the normal levels. The current view (Kallfelz, 1973; Hoge et al., 1974

Belshaw & Rijnberk, 1979; Bush, 1979) is that the greatest change is at 8 and 12 hours after an intramuscular injection of TSH and in normal dogs the increase in T4 is two- to three-fold or even more, whereas in primary hypothyroidism, it may be increased but is not doubled. The dogs have to be kept in hospital for the necessary period (Chastain, 1978). The interpretation of T3 assay, after TSH administration is less satisfactory but the T4 assay should separate the primary cases of hypothyroidism from other causes of low circulating T4 (Belshaw & Rijnberk, 1979).

If this procedure had been added to the considerable battery of investigations undertaken in the present research, it would have served the functions noted by Belshaw and Rijnberk (1979), i.e. it would have identified which of the dogs having low levels of circulating T4 were cases of primary hypothyroidism and which were not. It cannot be relied upon to distinguish cases of secondary hypothyroidism with the same degree of confidence. However, it could not simply have been undertaken in connection with, for example, the normal and the hypothyroid suspected groups alone. It would have been necessary to apply it to all the cases with levels of circulating T4 less than 1.5 mcg/100 ml.

Clearly the evidence from the present research is that cases of clinically suspected hypothyroidism and suspected cases of other hormonal disease such as

spontaneous and iatrogenic Cushing's disease in which low levels of T4 and T3 and elevated cholesterol levels occur, should not only have T4 and T3 assays routinely conducted, but if the levels are low the TSH stimulation test should also be applied. One should note, of course, that if there is a combination of features suggestive of the syndromes of hypothyroidism and Cushing's disease, this may indicate that these disorders are secondary to pituitary or hypothalamic dysfunction. In such cases, the response to TSH injection will be a rise in T4 but it should be less than two-fold. It is evident from the present research that the syndrome of pyoderma also requires further investigation. It would be worthwhile to study the thyroid status of such cases, making use of the TSH stimulation test where appropriate, to ascertain whether subclinical or mild clinical hypothyroidism is an influence in the aetiology of some cases. Of course, low levels of T4 need not necessarily indicate the presence of a subclinical disease. The low levels may be such that the dog is able to cope adequately and in such a case, it would be regarded as tolerant of the low level.

The broad based nature of the present research has raised questions which can only be answered by a further series of research projects.

The validity and sensitivity of the T4 RIA and T3 RIA assays employed in the present research require further consideration. When duplication of T4 and T3 assays was

carried out, there was a close agreement of the results for each of the tests. This indicated that the procedure was accurate whether it was undertaken on serum samples of unknown thyroid hormone concentration from the dogs under investigation, or from the standard control sera which were supplied with the test kits.

The question of whether the kits used are of sufficient sensitivity to provide meaningful results with sera containing T4 levels below, for example, 1 mcg/100 ml, as is the case in some dogs, is an important one. The kits are intended to measure the range of values found in man and this is higher than the range in the dog. Two procedures can be undertaken to estimate low values. One is to use double volumes of the serum being tested and a normal amount of radioactive material, as has already been described in this thesis. The result obtained when halved should indicate the true value. It is only necessary to perform the test in this modified way when the T4 or T3 concentration of the serum has already been shown by the unmodified method to be at or below the value of the lowest standard provided.

The second procedure that may be adopted to improve sensitivity, involves the use of control sera with very low thyroid hormone content. To produce this, serum is obtained from dogs known to have very low plasma T4 and T3 concentrations. This serum is then stripped of its thyroid hormone content by a charcoal absorption technique.

Measured amounts of thyroid hormone are then added to create the standards. By this procedure, sera with very low T4 and T3 concentrations become available and provide the standards against which the sera of unknown hormonal value may be compared. This second procedure was published in the spring of 1979 by Belshaw and Rijnberk by which time the present researches were largely completed. The lowest standards used in the present research were 0.6 mcg T4/ 100 ml and 0.03 ng T3/ml. In the present cases, lower levels than these were ascertained by using double volumes of the serum and extrapolation of the plotted curve below the points given by the lowest standards. Accordingly, it is likely that some of the values recorded below the standards are not sensitive indicators of these very low levels. Thus, in retrospect, it seems more appropriate to designate such values as "less than 0.6 mcg T4/ml" and "less than 0.03 ng T3/ml" respectively rather than as individual measurements. However, as values below 1.0 to 1.5 mcg T4/100 ml and below 0.5 ng T3/100 ml are generally regarded as indicative of hypothyroidism and the lowest standard sera used in the present work had values lower than these, the interpretations put forward in this thesis are not affected by using broad bands such as "less than 0.6 mcg T4/100 ml" and "less than 0.03 ng T3/ml", to identify the lowest values.

REFERENCES

REFERENCES

Acland, J.D. 1971. The interpretation of the serum protein bound iodine: A review. J. clin. Path., 24, 187-218.

Al-Bagdadi , F.A., Titkemeyer, C.W. and Lovell, J.E.1977. Hair follicle cycle and shedding in male beagle dogs. Am. J. vet. Res., 38, 611-616.

Amoroso, E.C. and Ebling, F.J. 1966. Allergic and endocrine dermatoses in the dog and cat-II. Hormones and skin. J. small Anim. Pract., 7, 755-775.

Anderson, J.J.B. and Dorner, J.L. 1971. Total serum thyroxine in thyroidectomised Beagles, using 125 I-labelled thyroxine, and comparison of T-3 and T-4 tests. J. Am. vet. med. Ass., 159, 760-762.

Anderson, R.S. 1973. Obesity in the dog and cat . In Grunsell, C.S.G. and Hill, F.W.G. (eds.) , Veterinary Annual 14th year. John Wright. Bristol. pp.182-186.

Anderson, R.S. 1976, personal communication.

Anderson, W.N. 1974. A treatment regimen for seborrhea of dogs. J.Am.vet.med.Ass., 164, 1111-1113.

Archer, H.E. and Robb, G.D. 1925. The tolerance of the body for urea in health and disease. Quart. J. Med. 18, 274-287.

Austin, V.H. 1974. Sebopsoriasis in the dog. Mod. Vet. Pract., 55, 379.

Bagnall, B.G. 1977. Recent advances in canine dermatology. In Grunsell, C.S.G. and Hill, F.W.G. (eds.). The Veterinary Annual 17th Issue. Scientechnica. Bristol. pp. 191-194.

Baker, H.J., 1971. Laboratory evaluation of thyroid function. In Kirk, R.W. (ed.). Current Veterinary Therapy IV small animal practice, W.B. Saunders, Philadelphia, pp. 595-602.

Baker, K.P. 1966. An Histological and Histopathological Study of the Skin of the Dog. PH.D. Thesis, University of Dublin.

Baker, K.P. 1974a. Hormonal alopecia in the dog and cat. Ir. vet. J., 28, 131-133. (clinical Annotation).

Baker, K.P. 1974b. Hair growth and replacement in the cat. Br.vet.J. 130, 327-334.

Barker, S.B. 1948. Determination of protein bound iodine. J. biol. Chem., 173, 715-724.

Barker, S.B. 1954. The circulating thyroid hormone. Brookhaven Symp-Biol. 7, 74-89.

Beierwaltes, W.H. and Nishiyama, R.H. 1968. Dog thyroiditis: occurrence and similarity to Hashimoto's Struma. - Endocrinology, 83, 501-508.

Bell, G.H., Emslie-Smith, D.and Paterson, C.R. 1976. Textbook of Physiology and Biochemistry, 9th ed. Churchill Livingstone. Edinburgh, London and New York.

Bellabarba, D. and Stirling, K. 1969. Formation of esters of T4 and T3 during alcoholic extraction. J. clin. Endocr. Metab., 29, 1510-1513.

Belshaw, B.E. 1962. Personal communication cited by Greve J.H. and Gaafar, S.M. 1964b.

Belshaw, B.E. 1967. Laboratory evaluation of thyroid function. Proc. 34th American Animal Hospital Association Meeting (N.Y.), 69-71.

Belshaw, B.E. 1968. Department of Medicine, Cornell University Medical College, New York, unpublished data cited by Bullock, L. 1970.

Belshaw, B.E. 1971. Hypothyroidism. In Kirk, R.W. (ed.). Current Veterinary Therapy IV Small Animal Practice, W.B. Saunders, Philadelphia. pp. 602-605.

Belshaw, B.E. 1975. Personal Communication, cited by Muller, G.H. and Kirk, R.W. 1976.

Belshaw, B.E., Barandes, M., Becker, D.V. and Berman, M. 1974. A model of iodine kinetics in the dog. Endocrinology, 95, 1078-1093.

Belshaw, B.E., Cooper, T.B. and Becker, D.V. 1975. The iodine requirement and influence of iodine intake on iodine metabolism and thyroid function in the adult beagle. Endocrinology, 96, 1280-1291.

Belshaw, B.E. and Rijnberk, A. 1977. Hypothyroidism. In Kirk, R.W. (ed.). Current Veterinary therapy VI small animal practice. W.B. Saunders. Philadelphia, pp. 1017-1019.

Belshaw, B.E. and Rijnberk, A. 1979. Radioimmuno-assay of plasma T4 and T3 in the diagnosis of primary hypothyroidism in dogs. J. Am. Anim. Hosp. Ass., 15, 17-23.

Benotti, J. and Benotti, N. 1963. protein bound iodine, total iodine and butanol-extractable iodine by partial automation. Clin. Chem., 9, 408-416.

Binswanger, F. 1936. Endokrinologie, 17: 22, 150, cited by Goldberg, R.C. and Chaikoff, I.L. 1952.

Blackburn, C.M. and Power, M.H. 1955. Diagnostic accuracy of serum protein bound iodine determination in thyroid disease. J. clin. Endocr. Metab.,15, 1379-1392.

Blackburn, P.S. 1965. The hair of cattle, horse, dog and cat. In Rook, A.J. and Walton, G.S. (eds.). Comparative physiology and pathology of the skin. Blackwell Scientific Publications, Oxford, pp.201-210.

Blake, S. and Lapinski, A. 1980. Hypothyroidism in different breeds, Canine practice, 7,

Blakemore, J.C. 1974. Endocrine disorders: Their influence on the integument. In Kirk, R.W. (ed.). Current Veterinary Therapy V: Small Animal Practice. W.B. Saunders, Philadelphia. pp. 448-457.

Bloom, F. 1959. In Hoskins, H.P., Lacroix, J.V. and Mayer. K. (eds). Revised by Bone, J.F. and Golick, P.F. Canine Medicine, 2nd Ed. American Veterinary Publications, Santa Barbara pp. 362-371.

Bloom, F. 1971. Diseases of the thyroid. In Catcott, E.J. (ed.). Canine Medicine, First Catcott edition. American Veterinary Publication, Inc. California. pp. 424-429.

Bold, A.M. and Browning, D.M. 1975. Quality control of thyroid function tests in vitro. J. clin. Path., 28, 234-238.

Borgman, R.F. and Reineke, E.P. 1949. The response of English bulldog puppies to thyroidal stimulation. J. Am. vet. med. Ass., 115, 480-486.

Borgman, R.F. and Reineke, E.P. 1950. The response of thyroidectomized and intact dogs to thyroidal stimulation. Am. J. vet. Res., 11, 149-156.

Bornfors, S. 1958. Acanthosis nigricans in dogs. Acta. endocr., Copenh., 28, suppl. 37, 9-63.

Boyd, G.S. and Oliver, M.F. 1958. The physiology of the circulating cholesterol and lipoproteins. In Cook, R.P. (ed.). Cholesterol, Chemistry, Biochemistry and Pathology, Academic Press, Inc. publishers. New York, pp. 181-208.

British Veterinary Association. 1961. Aspects of Skin Diseases of the Dog and Cat. BVA, London. pp. 1-72.

Brown, B.L., Ekins. R.P., Ellis, S.M. and Reith, W.S. 1970. Specific antibodies to triiodothyronine hormone. Nature, 226, 359.

Brown, B.L., Ekins, R.P., Ellis, S.M. and Williams, E.S. 1971. The radioimmunoassay of triiodothyronine. In Further Advances in Thyroid Research (6th International Conference) Edited by K. Fellinger and R. Hofer, Academy of Medicine, Vienna, p. 1107. Cited by Eastman, C.J., Corcoran, J.M., Ekins, R.P. Williams, E.S. and Nabarro, J.D.N. (1975).

Brunsch, A. 1956. Comparative investigations of the hair coat of wild and domesticated dogs. Z. Tierzucht. Zucht Biol., 67 (3), 205-240.

Bryan, G.M. 1960. Hypothyroid anemia in the canine. SWest Vet., 7, 66-68.

Bullock, L. 1970. Protein bound iodine determination as a diagnostic aid for canine hypothyroidism. J. Am. vet. med. Ass., 156, 892-899.

Burns, M. 1943. Hair pigmentation and the genetics of colour in greyhounds. Proc. R. Soc. Edinb., Section B (Biology) vol. 61 part 4 (No. 31).

Burns, M. 1978. Personal Communication.

Burr, W.A., Ramsden, D.B., Evans, S.E., Hogan T. and Hoffenberg, R. 1977. Concentration of thyroxine-binding globulin: value of direct assay. Br. med. J., I, 485-488.

Buser, J.C. 1974. Lipids and cholesterol in the healthy and sick dog. Schweizer Arch. Tierheilk., 116, 21-30 (in French). Abstract 2830, Vet. Bull., 1974, 44.

Bush, B.M. 1969a. Thyroid diseases in the dog - A review: part I. J. small Anim. Pract., 10, 95-109.

Bush, B.M. 1969b. Thyroid disease in the dog - A review: part II. J. small Anim. Pract., 10, 185-199.

Bush, B.M. 1970a. A Clinical and Experimental Evaluation of some Diagnostic Tests of Thyroid Function in the Dog. Ph.D. Thesis, University of London.

Bush, B.M. 1970b. The effect of dietary iodine on blood cholesterol levels in the dog. Res. vet. Sci., 11, 597-598.

Bush, B.M. 1972a. Naturally occurring thyroid disorders of the dog .In Grunsell, C.S.G. and Hill, F.W.G. (eds.). Veterinary Annual 13th year. John Wright. Bristol. pp. 161-165.

Bush, B.M. 1972b. Thyroid function tests in a group of euthyroid dogs. Res. vet. Sci., 13, 177-181.

Bush, B.M. 1972c. The treatment of canine acanthosis nigricans. J.Small Anim.pract., 13, 59-64.

Bush, B.M. 1975. Veterinary Laboratory Manual. London: William Heinemann Medical Book Co.

Bush, B.M. 1977. The diagnosis of canine hypothyroidism. Proceeding of the 6th World Small Animal Veterinary Association, Amsterdam. Netherlands., Royal Netherlands Veterinary Association, pp. 102-103.

Bush, B.M. 1978. The influence of the thyroid gland on animal skin. Veterinary Dermatology Newsletter. 3(1), 8 - 11.

Bush, B.M. 1979. Endocrine system .In Chandler, E.A. Evans, J.M., Sing Leton, W.B., Startup, F.G., Sutton, J.B. and Tavernor, W.D. (eds.). Canine Medicine and Therapeutics. Blackwell Scientific Publication for the British Small Animal Veterinary Association, Oxford. pp. 166-189.

Bush, B.M. 1980 . The laboratory evaluation of canine hepatic disease .In Grunsell, C.S.G. and Hill, F.W.G. (eds.). Veterinary Annual 20th issue Scientechnica. Bristol. pp. 57-65.

Busted, L.R. and Fuller, J.M. 1970. Thyroid function in domestic animals. Laboratory Animal Care, 20, 561-581.

Capen, C.C., Belshaw, B.E. and Martin, S.L. 1975. Endocrine disorders.In Ettinger, S.J. (ed.). Textbook of Veterinary Internal Medicine, Diseases of the Dog and Cat, vol. 2, W.B. Saunders, Philadelphia. pp. 1351.1452.

Carr, E.A., Beierwaltes, W.H., Raman, G., Dodson, V.N., Tanton, J. Betts, J.S. and Stambaugh, R.A. 1959. The effect of maternal thyroid function on fetal thyroid function and development. J. clin. Endocr. Metab., 19, 1 - 18.

Chaikoff, J.L., Entenman, C., Changus, G.W. and Reichert, F.L. 1941. Influence of thyroidectomy on blood lipids of the dog. Endocrinology, 28, 797-805.

Chastain, C.B. 1978. Human thyroid stimulating hormone radioimmunoassay in the dog. J. Am. Anim. Hosp. Ass., 14, 368-369.

Chester, D.K., Hightower, D., Kyzar, J.R. and Wright, E.M. 1974. T4, T3 uptake, T7 and cholesterol values in radiothyroidectomized beagles. SWest Vet. 27, 183-187.

Clark, F. 1975. Serum protein bound iodine or total thyroxine. J. clin. Path., 28, 211.217.

Clark, S.T. and Meier, H. 1958. A clinico-pathological study of thyroid disease in the dog and cat. part 1: Thyroid pathology. Zentbl. VetMed., 5(1), 2-32.

Cline, M.J. and Berlin, N.I. 1963. Erythropoiesis and red cell survival in the hypothyroid dog. Am. J. Physiol., 204, 415-418.

Coffin, D.L. and Munson, T.O. 1953. Endocrine diseases of the dog associated with hair loss. Sertoli cell tumor of testis, hypothyroidism, canine Cushing's syndrome. J. Am. vet. med. Ass., 123, 402-408.

Collins, R.D. 1975. Illustrated Manual of Laboratory Diagnosis. Indication and Interpretation, 2nd Ed. J.B. Lippincott. Philadelphia.

Comben, N. 1951. Observations on the mode of growth of the hair of the dog. Br.Vet.J., 107, 231-235

Conroy, J.D. 1979. Dermatopathologic signs of internal causation .In Muller, G.H. (ed.). The Veterinary Clinics of North America. Vol. 9(1), W.B. Saunders Co., Philadelphia, pp. 133-140.

Cook, R.P. 1958. Distribution of sterols in organisms and in tissue, in Cholesterol, Chemistry, Biochemistry and Pathology. Academic Press, Inc. publishers, New York. pp. 145-180.

Crispell, K.R. Kahana, S. and Hyer, H. 1956. The effect of plasma on the in vitro uptake or binding by human red cells of radioactive ^{131}I-labelled L-thyroxine and L-triiodothyronine. J. clin. Invest., 35, 121-124.

Crispin, S.M. and Barnett, K.C. 1978. Arcus lipoides cornea secondary to hypothyroidism in the Alsatian. J. small. Anim. Pract., 19, 127-142.

Cuaron, A. 1969. Determination of serum thyroxine by saturation analysis of thyroxine binding proteins. J. nucl. Med., 10, 532-539.

Dacie, J.V. and Lewis, S.M. 1975. Practical Haematology. Fifth Ed. Churchill Livingstone. pp 41-43.

Dall, J.A. 1958. A practitioner's approach to skin diseases in small animals. Vet. Rec., 70, 1029-1039.

Danowski, T.S., Man, E.B. and Winkler, A.W. 1946. Tolerance of normal, of thyroidectomized and of thiourea or thiouracil treated dogs to oral, dessicated thyroid and to intravenous thyroxine. Endocrinology, 38, 230-237.

Danowski , T.S., Wirth, P., Black, M.H., Barton, E. and Bastiani, R.M. 1955. Effects of vitamin A supplements on serum protein bound iodine (PBI) level, and disposal of exogenous thyroxine. J. clin. Endocr. Metab., 15, 1262-1269.

Davies, A.G. 1972. Thyroid physiology. Br. med. J., 2, 206-209.

Davies, T. 1975. Personal Communication cited by Muller, G.H., and Kirk, R.W. 1976.

Dimopoullos, G.T. 1963. Plasma Proteins .In Cornelius, C.E. and Kaneko, J.J. (eds.). Clinical Biochemistry of Domestic Animals. Academic Press, New York, 1st Ed. pp. 109-188.

DiScala, V.A., Lippe, R.D. and Segal, R.L. 1971. A simple, reliable method for producing hypothyroidism in the dog and thyroid function tests in normal and hypothyroid dog. Endocrinology, 88, 504-506.

Dott, M. 1923. An investigation into the functions of the pituitary and thyroid glands. Part 1. Technique of their experimental surgery and summary of results. Q.J. exp. Physiol., 13, 241-282.

Doxey, D.L. 1971. Veterinary clinical pathology, Bailliere Tindall, London, pp. 356.

Doxey, D.L. 1978. Personal communication.

Durward, A. and Rudall, K.M. 1949. Studies on hair growth in the rat. J. Anat., 83, 325-335.

Eastman, C.J., Corcoran, J.M., Ekins, R.P., Williams, E.S. and Nabarro, J.D.N. 1975. The radioimmunoassay of triiodothyronine and its clinical application. J. clin. Path., 28, 225-230.

Ebling, F.J. 1965. Comparative and evolutionary aspects of hair replacements .In Rook, A.J. and Walton, G.S. (eds.). Comparative Physiology and Pathology of the Skin. Blackwell Scientific Publications, Oxford. pp. 87-102.

Edney, A. 1972. Current trends in small animal nutrition. In Grunsell C.S.G. and Hill, F.W.G. (eds.). Veterinary Annual, 13th year. John Wright, Bristol, pp. 194-199.

Ekman, L. 1976. Variation of some blood biochemical characteristics in cattle, horses and dogs and causes of such variations. Ann. Rech. Vet., 7, 125-128.

Ekman, L. and Orstadius, K. X Nord Vet Mofet., Stockholm. 1966, 486. Cited by Orstadius, K. 1971.

Ekman, L., Orstadius, K. and Thorell, C.B. 1968. Canine thyroid function in adiposity and certain skin ailments studied by the EU test. J. small Animal Pract., 9, 225-230.

Ekman, L. and Thorell, C.B. 1965. Studies on in vitro erythrocyte uptake of 1^{131} labelled I-triiodothyronine as a test of thyroid function in dairy cattle. Acta vet. Scand., 6, 30-40.

Elking, M. and Karat, H. 1968. Drug induced modifications of laboratory test values. Amer. J. Hosp. Pharm., 25, 484.

Ettinger, S.J. 1975. Textbook of Veterinary Internal Medicine. Diseases of the Dog and Cat. Vol. 2. W.B. Saunders Company, Philadelphia, London, Toronto.

Evered, D.C. 1976 Diseases of the thyroid. Pitman Medical Publishing Co., London.

Farran, H.E.A. and Bush, B.M. 1971. Hormonal iodine in the dog. J. Endocr., 51, 417-424.

Farrell, L.P. and Richmond, M.H. 1961. A rapid method for the estimation of serum protein bound iodine. Clinica chim. Acta, 6, 620-623.

Fowler, P.B.S. 1977. Subclinical hypothyroidism. Br. med. J., 1, 447.

Fredrickson, D.S., Ganong, W.F. and Hume, D.M. 1955. Thyroid uptake of radioactive iodine in the dog. Proc. Soc. exp. Biol. Med., 89, 415-420.

Freudiger, U. 1960. Alopecia and the thyroidea hormone. Berl. Munch. tierarztl. Wschr., 73, 28-30. (in German, English summary).

Freudiger, U. 1962. Klinik und Funktionelle Pathologie der Schilddruse. Schweizer Arch. Tierheilk, 104, 638-649. (English summary).

Frey, H.M.M. 1967. Peripheral circulatory and metabolic consequences of thyrotoxicosis. I. Blood flow and oxygen consumption of resting and working skeletal muscle in experimental thyrotoxicosis in the dog. Scan. J. clin. Lab. Invest., 19, 4-14.

Furth, E.D. Becker, D.V., Nunez, E.A. and Reid, C.F. 1968. Thyroxine metabolism in the dog. Endocrinology, 82, 976-982.

Glock, G.E. 1949. Effect of the administration of thiouracil to dogs. J. Endocr., 6, 6-13.

Godden, J.D. and Garnett, E.S. 1964. The ^{131}triiodothyronine resin uptake test. J. Endrocr., 29, 167-174.

Goldberg, R.C. and Chaikoff, I.L. 1952. Myxedema in the radiothyroidectomised dog. Endocrinology, 50, 115-123.

Goldie, D.J., Jennings, R.D. and McGowan, G.K., 1974. The estimation of a serum thyroxine by competitive binding analysis: a modified method. J. clin. Path., 27, 74-82.

Goolden, A.W.G., Gartside, J.M. and Orsorio, C. 1965. An evaluation of the ^{131}-I-triiodothyronine resin sponge test. J. clin. Endocr. Metab., 25, 127-133.

Gosselin, S., Capen, C.C., and Martin, S.L. 1978. Hashimoto's thyroiditis. Animal model : Lymphocytic thyroiditis in the dog. Am.J.Path., 90, 285-288.

Gould, R.G., Taylor, C.B., Hagerman, J.S., Warner, I. and Campbell, D.J. 1953. 1. Effect of dietary cholesterol on the synthesis of cholesterol in dog tissue in vitro. J. biol. Chem., 201, 519-528.

Goyings, L.S. 1961-62. Hypothyroidism and skin diseases. Gaines Dog Research Prog. pp. 1-3.

Goyings, L.S., Reineke, E.P. and Schirmer, R.G. 1962. Clinical diagnosis and therapy of hypothyroidism in dogs. J. Am. vet. med. Ass., 141, 341-347.

Greene, J.A., Knecht, C.D. and Roesel, O.F. 1979. Hypothyroidism as a possible cause of canine intervertebral disk disease. J. Am. Anim. Hosp. Ass., 15, 199-202.

Gregor, W.W. 1965. The incidence of skin diseases in small animal practice. In Rook, A.J. and Walton, G.S. (eds.). Comparative Physiology and Pathology of the Skin. Blackwell Scientific Publications, pp. 33-69.

Greve, J.H. and Gaafar, S.M. 1964a. Effect of hypothyroidism on canine demodicosis. Am. J. Vet. Res., 25, 520-522.

Greve, J.H. and Gaafar, S.M. 1964b. Radiotriiodothyronine for the evaluation of experimentally induced hypothyroidism in dogs. Am. J. vet. Res., 25, 1191-1194.

Grigaut, A. and L'Huillier, A. 1912. Hypercholesterinemie d'origine alimentaire chez le chien. C. r. Seanc Soc. Biol. Par., LXXIII, 304-307.

Gross, J. and Leblond, C.P. 1951a. Metabolites of Thyroxine. Proc. Soc. exp. Biol. Med., N.Y., 76, 686-689.

Gross, J. and Leblond, C.P. 1951b. The presence of free iodinated compounds in the thyroid and their passage into the circulation. Endocrinology, 48, 714-725.

Gross, J. and Pitt-Rivers, R. 1951. Unidentified iodine compounds in human plasma in addition to thyroxine and iodide. Lancet, 2, 766-767.

Gross, J. and Pitt-Rivers, R. 1951-52. Experimental study of thyroid metabolism with radioactive iodine. Br. med. Bull., 8, 136-140.

Gross, J. and Pitt-Rivers, R. 1952a. The identification of 3:5:3-L-triiodothyronine in human plasma. Lancet, 1, 439-441.

Gross, J. and Pitt-Rivers, R. 1952b. Physiological activity of 3-5-3-L-triiodothyronine. Lancet, 1, 593-594.

Gross, J. and Pitt-Rivers, R. 1953a. 3:5:3-L-triiodothyronine. 1. Isolation from thyroid gland and synthesis. Biochem. J., 53, 645-650.

Gross, J. and Pitt-Rivers, R. 1953b. 3:5:3 L-triiodothyronine. 2. Physiological activity. Biochem. J., 53, 652-657.

Groth, W. 1962a. In Handbuch der Speziellen Pathologischen Anatomie der Haustiere 3rd Ed., vol. 4 (Eds. Dobberstein, J., Pallaske, G. and Stunzi, H.) pp. 1-48. Paul Parey, Berlin. Cited by Bush, B.M. 1969a.

Groth, W. 1962b. The pathology of goitre and thyroid tumours of domestic animals. Dt. tierarztl. Wschr., 69, 707-713. (in German, English summary).

Hamburger, J.I. 1970. Thyroid tests: two thyroid tests (T3, T4) may be better than one protein bound iodine. Medical News. J.Am.med.Ass., 211, 579.

Hamlin, R.L., Olsen, I., Smith, C.R. and Boggs, S. 1967. Clinical relevancy of heart rate in the dog. J. Am. vet. med. Ass., 151, 60-63.

Hamolsky, M.W., Stein, M. and Freedberg, A.S. 1957. The thyroid hormone-plasma protein complex in man. 11. A new in vitro method for study of 'uptake' of labelled hormonal components by human erythrocytes. J. clin. Endocr. Metab., 17, 33-44.

Hamolsky, M.W., Golodetz, A. and Freedberg, S. 1959. The plasma protein-thyroid hormone complex in man. III. Further studies on the use of the in vitro red blood cell uptake of ^{131}I-triiodothyronine as a diagnostic test of thyroid function. J. clin. Endocr. Metab., 19, 103-116.

Harington, C.R., 1926. Chemistry of throxine. II. Constitution and synthesis of desiodo-thyroxine. Biochem. J., 20, 300-313.

Harington, C.R.and Barger, G. 1927. Chemistry of thyroxine. III. Constitution and synthesis of thyroxine. Biochem. J., 21, 169-181.

Hathway, J.E. 1974. Anaemia in the dog .In Kirk, R.W.(ed.). Current Veterinary Therapy, V: Small Animal Practice, W.B. Saunders, Philadelphia, pp. 347-349.

Hauck, E. 1949. Skin thickness in the dog. Wien tierarzt. Mschr.,36, 670-674.

Havard, C.W.H. 1974. Which test of thyroid function? Br. med. J., 1, 553-556.

Hightower, D., Kyzar, J.R., Chester, D.K. and Wright, E.M. 1973a. In vitro thyroid function test: results during replacement therapy in hypothyroid beagle dogs. Veterinary Medicine and Small Animal Clinician, 68, 1131-1132.

Hightower, D., Kyzar, J.R., Chester, D.K. and Wright, E.M. 1973b. Replacement therapy for induced hypothyroidism in dogs. J. Am. vet. med. Ass., 163, 979-980.

Hightower, D., Kyzar, J.R., Chester, D.K. and Wright, E.M. 1974. Hypothyroid test result in normal dogs. SWest Vet. 27, 155-159.

Hightower, D. and Miller, L.F. 1969. Thyroid function tests in veterinary medicine, 1. A review. SWest.Vet. 22, 200-205.

Hightower, D., Miller, L.F. and Kyzar, J.R. 1969. Thyroid function tests in veterinary medicine, II. Results and applications. SWest. Vet., 23, 15-22.

Hoe, C.M. and Harvey, D.G. 1961. An investigation into liver function tests in dogs. Part 2. Tests other than transaminase estimations. J. small Anim. Pract., 2, 109-127.

Hoe, C.M. and O'Shea, J.D. 1965. The correlation of biochemistry and histopathology in liver disease in the dog. Vet. Rec., 77, 1164-1171.

Hoffenberg, R. 1975. The present role of in vitro tests of thyroid function. J. clin. Path., 281 239-243.

Hoffenberg, R. 1977. Diseases of the thyroid. Br. med. J., 1, 176.

Hoffer, R.E. 1962. A clinical case of hypothyroidism in the dog. Auburn Vet., 18, 73-76.

Hoge, W.R., Lund, J.E. and Blakemore, J.C. 1974. Response to thyrotropin as a diagnostic aid for canine hypothyroidism. J. Am. Anim. Hosp. Ass., 10, 167-170.

Hollander, C.S., Thompson, R.H., Barrett, P.V.D. and Berlin, N.I. 1967. Repair of the anemia and hyperlipidemia of the hypothyroid dog. Endocrinology, 81, 1007-1017.

Holmes, J.W.H. 1933. Canine and feline skin diseases. Vet. Rec., 13, 603-609.

Horn, D.B. 1974. Available assays for serum thyroxine and for serum uptake tests. J.Clin.path.,28, 218-224.

Hubbard, C.L.B. 1964. The Observer's Book of Dogs, Warne, London and New York.

Hullinger, R.L. 1979. The endocrine system.In Miller's Anatomy of the Dog. Evans, H.E. and Christensen, G.C. (eds.). W.B. Sunders Co. Philadelphia, pp. 611-615.

Ihrke, P.J. 1979. Canine seborhheic diseases complex. Symposium on skin and internal diseases. Veterinary Clinics of North America, 9, (1), 93-106.

Irvine, C.H.G. 1967. Protein bound iodine in the horse. Am. J. vet. Res., 28, 1687-1692.

Jasper, D.E. and Jain, N.C. 1965. Effects of lipemia upon erythrocyte fragility, sedimentation rate, and plasma refractrometer indexes in the dog. Am. J. vet. Res. 26, 332-338.

Joshua, J.O. 1958. Non-parasitic skin diseases of the dog and cat. Vet. Rec., 70, 193-198.

Jovanovic, M., Pantic, V. and Djurdjevic, D.J. 1959. Functional and morphological changes in thyroid gland and hypophysis in castrated rats. Proc. 16th Int. Vet. Cong. 2, 45-46.

Jubb, K.V.F. and Kennedy, P.C. 1963. Pathology of Domestic Animals, 1st Ed., Academic Press, New York. Vol. 1 pp. 321-330.

Jubb, K.V.F. and Kennedy, P.C. 1970. The endocrine glands. In Jubb, K.V.F. and Kennedy, P.C. (eds.). Pathology of Domestic Animals, 2nd Ed., Vol. I, pp. 407-418. Academic Press, New York.

Kaihara, S., Carullit, N and Wagner, H.N. 1969. Comparison of radioisotopic and column chromatographic assay of serum thyroxine. J. nucl. Med., 10, 281-283.

Kallfelz, F.A. 1968. The triiodothyronine ^{131}I resin sponge uptake test as an indicator of thyroid function in dogs. J. Am. vet. med. Ass. 152, 1647-1650.

Kallfelz, F.A. 1969a. Comparison of the ^{125}I T3 and ^{125} T4 tests in the diagnosis of thyroid gland function in the dog. J. Am. vet. med. Ass. 154, 22-25.

Kallfelz, F.A. 1969b. Determination of total serum thyroxine in the dog by competitive protein binding of labeled thyroxine. Am. J. vet. Res., 30, 929-932.

Kallfelz, F.A. 1973. Observations on thyroid gland function in dogs: response to thyrotropin and thyroidectomy and determination of thyroxine secretion rate. Am. J. vet. Res., 34, 535-538.

Kallfelz, F.A. 1977. Thyroid function in the dog. Symposium on endocrinology. Veterinary Clinics of North America, 7, (3), 497-512.

Kallfelz, F.A., Comar, C.L. and Wentworth, R.A. 1974. Veterinary nuclear medicine. Adv. in Vet. Sci. Comp. Med.,18, 55-78.

Kallfelz, F.A. and Erali, R.P. 1973. Thyroid function tests in domesticated animals: free thyroxine index. Am. J. vet. Res.,34, 1449-1451.

Kaneko, J.J. 1960. Tests of thyroid function. Calif. Vet., 14, (1), 32-33.

Kaneko, J.J. 1963. Selected organ function tests .In Cornelius, C.E. nad Kaneko, J.J. (eds.). Clinical Biochemistry of Domestic Animals, Academic Press, London, pp. 310-317.

Kaneko, J.J. 1969. Personal communication, cited by Muller, G.H. and Kirk, R.W. 1976.

Kaneko, J.J. 1970. Thyroid function .In Kaneko, J.J. and Cornelius, C.E. (eds.). Clinical Biochemistry of Domestic Animals. 2nd Ed. Vol. I. Academic Press, New York. pp. 293-311.

Kaneko, J.J. 1979. Cited by Ling et al. (1979)

Kaneko, J.J., Baker, B. and Mills, R. 1975. Laboratory evaluation of the canine thyroid gland AVMA Annual Meeting - American Society of Veterinary Clinical Pathologists, Anaheim, Calif., July Bull. of the Am. Soc. of Vet. Clin. Path., 4 (3 and 4), p. 30.

Kaneko, J.J., Tyler, W.S., Wind, A. and Cornelius, C.E. 1959 Clinical applications of the thyroidal ^{131}I uptake test in the dog. J. Am. vet. med. Ass., 135, 516-520.

Kelley, S.T. and Oehme, F.W. 1974. Circulating thyroid levels in dogs, horses and cattle. Veterinary Medicine Small Animal Clinician, 69, 1531-1533.

Kelley, S.T., Oehme, F.W. and Hoffman, S.B. 1974. Evaluation of selected commercial thyroid function tests in dogs. Am. J. vet. Res., 35, 733-736.

Kelly, D.F. and Darke, P.G.G. 1976. Cushing's syndrome in the dog. Vet. Rec., 98, pp. 28-30.

Kelsey, F.O., Gullock, A. and Clausen, H.J. 1960. Plasma protein bound iodine in the beaver and other animals. Acta Endocr., Copenh., 35, 495-500.

Kendall, E.C. 1915. A method for the decomposition of the proteins of the thyroid, with a description of certain constituents. J. biol. Chem., 20, 501-509.

Kiesel, G.K. and Burns, M.J. 1960. A preliminary report on the serum protein bound iodine in dairy cattle. Am. J. vet. Res., 21, 226-229.

Kirk, H. 1947. Index of Diagnosis, 3rd Ed. Balliere, Tindall and Cox, London. pp. 287, 464-465. Cited by Bush, B.M. 1969a.

Kirk, R.W. 1971. Alopecia. Scientific Presentation and Seminar Synopses of the 38th Ann. Meeting, Am. Anim. Hosp. Ass., Apr. 25-30, pp. 218-219.

Kirk, R.W. 1979. Acanthosis nigricans. Symposium on the skin and internal diseases. Veterinary Clinics of North America, 9, (1), pp. 49-56.

Klatt, B. 1948. Wuchsform und Hypophyse. Wilhelm Roux Arch. Entw. Mech., 143, 167-179.

Komarova, T.F., Sokolova, E.V. and Tendler, D.S. 1965. Uroven' sviazannogos belkom ioda krovi u sobak s razlichnymi sovistvami nervnykh protesessov. Zh. vyssh. nerv. deyat. I.P. Pavlova 15, 114-119. Cited by Bush, B.M. 1970a.

Kraft, W. 1975. Diagnosis of thyroid disease in the dog. (Zur Diagnostik von Schildrusener-vrakungen beim Hund) Kleintier-Prax 20, 84-88.

Kraft, W. 1976. Thyroid Function Disturbances in the Dog. (Translated title), Thesis, Justus Liebig. Univ., Giessen, W. Germany, (in German), cited by Belshaw, B.E. and Rijnberk, A. 1979.

Kraft, W. and Gerbig, T. 1977. Studies on the stimulation test using thyrotropin releasing hormone (TRH) in the dog. Dt. tiervarztl Wschr., 84, 185-187.

Kral, F. and Schwartzman, R.M. 1964. The thyroid .In Veterinary and Comparative Dermatology, J.B. Lippincott Co., Philadelphia, pp. 68-70.

Kristensen, S. 1975a. A study of skin diseases in dogs and cats. I. Histology of the hairy skin of dogs and cats. Nord. VetMed., 27, 593-603.

Kristensen, S. 1975b. Thyroxine responsive alopecia in the dog. Dansk Vejtidsskr., 58, 730-733.

Kronfeld, D.S., Johnson, K. and Dunlap, H. 1979. Inherited predisposition of dogs to diet-induced hypercholesterolemia. J. Nutr., 109, 1715-1719.

Kurland, G.A., Hamolsky, M.W. and Freedberg, A.S. 1955. Studies in non-myxedematous hypometabolism; clinical syndrome and effects of triiodothyronine alone or combined with thyroxine. J. clin. Endocr. Metab., 15 1354-1366.

Kyzar, J.R., Chester, D.K. and Hightower, D. 1972. Comparison of T3, T3 tests and radioactive iodine uptake determination in the dog. Veterinary Medicine. Small Animal Clinician 67 321-322.

Larsson, M. and Lumsden, J.H. 1980. Evaluation of an enzyme linked immunosorbent assay (ELISA) for determination of plasma thyroxine in dogs. Zentbl. VetMed.,A 27, 9-15.

Lee, M., Tietz, N.W. and Martinez, C.J. 1972. Clinical evaluation of modified 'Oxford T4 - by column' method for serum thyroxine. Clin. Chem.,18, 422-426.

Lerman, J. 1940. Iodine components of the blood. Circulating thyroglobulin in normal persons and in persons with thyroid disease. J. clin. Invest.,19, 555-560.

Lewis, H.B. 1977. Management of anemia in the dog and cat. In Kirk, R.W. (ed.). Current Veterinary Therapy VI: Small Animal Practice. W.B. Saunders, Philadelphia pp. 421-430.

Lewis, L.A., Page, I.H. and Kolff, W.J. 1958. Serum lipoprotein and cholesterol changes in nephrectomized dogs maintained by peritoneal dialysis. Am. J. Physiol., 195, 161-165.

Li, T.W. and Freeman, S. 1946. Experimental lipemia and hypercholesterolemia by protein depletion and by cholesterol feeding in dogs. Am. J. Physiol., 145 660-666.

Lievre, E. 1976. Contribution a l'Etude de l'hypothyroidisme chez le Chien. Doctoral thesis, Alfort.

Ling, G.V., Stabenfeldt, G.H., Comer, K.M., Gribble, D.H. and Schechter, R.D. 1979. Canine hyperadrenocorticism: pretreatment clinical and laboratory evaluation of 117 cases. J. Am. Vet. Med. Ass., 174, 1211-1215.

Lippincott, S.W., Lewallen, C.G. and Shellabarger, C.J. 1957. Pathology of radioisotopic ablation of the thyroid in the dog. Archs Path., 63, 540-556.

Lombardi, M.H., Comar, C.L. and Kirk, R.W. 1962. Diagnosis of thyroid gland function in the dog. Am. J. vet. Res., 23, 412-420.

Lorenz, M.D. and Cornelius, L.M. 1976. Laboratory diagnosis of the endocrine diseases. Symposium on Clinical Laboratory Medicine. The Veterinary Clinics of North America,6,(4), 687-722.

Maahs, R.L. 1958-1959. Hypothyroidism in the dog. Iowa St. Coll. Vet.,27, 27-28.

McCullagh, K.G. 1978. Plasma lipoproteins in animal health and disease .In Grunsell, C.S.G. and Hill, F.W.G. (eds.). Veterinary Annual 18th issue. Scientechnica. Bristol pp. 41-50.

McGowan, G.K. 1975. Nomenclature. J. clin. Path. 28, 207-210.

Mahley, R.W., Weisgraber, K.H. and Fry, D.L. 1973. Canine lipoproteins and atherosclerosis. Fedn. Proc. Am. Soc. exp. Biol. 32, 294.

Mahley, R.W., Weisgraber, K.H. and Innerarity, T. 1974. Canine lipoproteins and athersclerosis. II. Characterisation of the plasma lipoproteins associated with atherogenic and nonatherogenic hyperlipidemia. Circulation Res., 35, Supp. 2 and 3, pp. 722-733.

Malherbe, W.D. 1965. Clinico-pathological studies of Babesia canis infection in dogs, III. J.S. Afr. vet. med. Ass.,36, 179 - 182.

Mallo, G.L. 1966. Cutaneous manifestation of canine hypothyroidism. Iowa St. Vet. Coll. 28 4-6.

Mallo, G.L. and Harris, A.L. 1967. ^{131}I triiodothyronine resin uptake, serum protein bound iodine and serum cholesterol tests in normal dogs. Veterinary Medicine Small Animal Clinician,62, 533-540.

Manning, P.J. 1979. Thyroid gland and arterial lesions of beagles with familial hypothyroidism and hyperlipoproteinemia. Am. J. vet. Res.,40, 820-828.

Manning, P.J., Corwin, L.A. and Middleton, C.C. 1973. Familial hyperlipoproteinemia and thyroid dysfunction of beagles. Exp. and Mol. Path.,19, 379-388.

Mann, G.V. and Stare, F.J. 1954. Nutrition and atherosclerosis, in Symposium on Atherosclerosis, Wash., D.C.: National Academy of Sci., Natn. Res. Coun., 169-180.

Marsden, P., Facer, P., Acosta, M. and Howorth, P.J.N. 1975. A comparative study of serum total thyroxine estimation on unextracted serum by radioimmunoassay and by competitive protein binding. J. clin. Path.,28, 608-612.

Martin, S.L. and Capen, C.C. 1979. Hypothyroidism and the skin. Symposium on the Skin and Internal Disease. Veterinary Clinics of North America 9 (1), pp. 29-39.

Mason, R. and Wilkinson, J.S. 1973. The thyroid gland - a review. Aust. Vet. J., 49, 44-49.

Mattingly, D. 1962. Cited by Varley, H. 1967.

Mawdesley-Thomas, L.E. 1968. Lymphocytic thyroiditis in the dog. J. small Anim. Pract.,9, 539-550.

Mayer, E. 1947. Inhibition of thyroid function in beagle puppies by propylthiouracil without disturbance of growth or health. Endocrinology,40, 165-181.

Meier, H. and Clark, S.T. 1958. The clinicopathological aspect of thyroid disease in the dog and cat. Part II: Clinical features. Zentbl. VetMed.,5 (2), pp. 120-128.

Michaelson, S.M. 1969. Assessment of canine thyroid function (valuable yet seldom used technics). Mod. vet. Pract.,50, 43-46.

Michaelson, S.M. and Quinlan, W. (JR), Casarett, J.W. and Mason, W.B. 1967. Radiation-induced thyroid dysfunction. Radiat. Res., 30, 38-47.

Mitchell, M.L., Harden, B.A. and O'Rourke, 1960. The in vitro resin sponge uptake of triiodothyronine 131 I - from serum in thyroid disease and in pregnancy. J. clin. Endocr. Metab., 20, 1474-1483.

Mitsuma, T., Nihei, N., Gershengorn, M.C. and Hollander, C.S. 1971. Serum triiodothyronine: measurements in human serum by radioimmunoassay with corroboration by gas-liquid chromatography. J. clin. Invest., 50, 2679-2688.

Moser, J.E. 1966. Dermatoses related to endocrine imbalance in the canine. Iowa Vet., 37, 7-10.

Muller, G.H. 1965. Hormonal dermatoses .In Scientific Presentations on Seminar Synopses, 32nd Annual Meeting, American Animal Hospital Association, cited by Mallo, G.L. 1966.

Muller, G.H. and Kirk, R.W. 1969. Small Animal Dermatology. W.B. Saunders, Philadelphia.

Muller, G.H. and Kirk, R.W. 1976. Small Animal Dermatology. 2nd Ed. W.B. Saunders, Philadelphia.

Munson, T.O. and Belshaw, B.E. 1966-67. Hypothyroidism . In Kirk, R.W. (ed.). Current Veterinary Therapy. Small Animal Practice. W.B. Saunders Co., Philadelphia. pp. 326-329.

Munzer, B., Hartung, K. and Blaurock, H.M. 1976. Radio-isotope testing for thyroid function tests in the dog. Determination of normal values. Berl. Munch. Tierarztl. Wschr., 89, 437-441. (In German, English Summary).

Murphy, B.E.P. and Jachan, C. 1965. The determination of thyroxine by competitive protein binding analysis employing an anion-exchange resin and radiothyroxine. J. Lab. clin. Med. 66, 161-167.

Murphy, B.E.P. and Pattee, C.J. 1964. Determination of thyroxine utilising the property of protein binding. J. clin. Endocr. Metab.,24, 187-196.

Murphy, B.E.P., Pattee, C.J., and Gold, A. 1966. Clinical evaluation of a new method for the determination of serum thyroxine. J. clin. Endocr. 26, 247-256.

Musser, E. and Graham, W.R. 1968. Familial occurrence of thyroiditis in purebred beagles. Lab. Anim. Care, (Baltimore) 18, 58-68.

Nunez, E.A., Becker, D.V., Furth, E.D., Belshaw, B.E. and Scott, J.P. 1970. Breed differences and similarities in thyroid function in purebred dogs. Am. J. Physiol., 218, 1337-1341.

Ojemann, J.G. 1940. Tijdschr. Diergeneesk. 67, 979, cited by Bush, B.M. 1969a.

O'Neal, L.W. and Heinbecker, P. 1953. The response of the plasma protein bound iodine of hypophysectomized dogs to injected thyrotropin: the influence of cortisone. Endocrinology,53, 60-72.

O'Neal, L.W. and Simms, E.S. 1953. Determination of protein bound iodine in plasma or serum, a simple and rapid method. Am. J. clin Path., 23, 493-505.

Orstadius, K. 1971. Differential diagnosis methods by hypothyreotic alopecia and some other kinds of alopecia in dog. 19th World Vet. Cong. Mexico City, 3, 1045-1050.

Parris, L.S. and Parris, R.G. 1966. Liothyronine in the diagnosis and management of hypothyroidism. Veterinary Medicine. Small Animal Clinician,61, 1080-1082.

Paul, P., Donohue, M. and Holmes, W.L. 1975. Glucose metabolism in thyroidectomized and normal dogs during rest and acute cold exposure. J. Appl. Physiol., 38, 236-240.

Pileggi, V.J. and Kessler, G. 1968. Determination of organic iodine compounds in serum: IV. a new non-incineration technic for serum thyroxine. Clin. Chem. 14, 339-347.

Pileggi, V.J., Lee, N.D., Gloube, O.J. and Henry, R.J. 1961. Determination of iodine compounds in serum: 1. Serum thyroxine in the presence of some iodine contaminants. J. clin. Endocr. Metab.,21, 1272-1279.

Pitt-River, R.V. and Tata, J.R. 1959. Physiological actions of thyroid hormones .In The Thyroid Hormones, London, Pergman Press, pp. 59-98.

Power, B.S. and Luzio, N.R.O. 1958. Dietary cholesterol and adrenal regulation of plasma lipids. Am. J. Physiol., 195, 116-170.

Premachandra, B.N. 1976. Cited by Premachandra, B.N. and Lang, S. 1977.

Premachandra, B.N. and Ibrahim, 1976, cited by Premachandra, B.N. and Lang, S. 1977.

Premachandra, B.N. and Lang, S. 1977. Circulatory reverse triiodothyronine (r T3) in the dog. Life Sci., 20, 1449-1454.

Quinlan, W. and Michaelson, S.M. 1967. Iodine ^{131} uptake and protein bound iodine in normal adult beagles. Am. J. vet. Res.,28, 179-182.

Quinlan, W.J., Thomson, R.A.E. and Michaelson, S. 1969. In vitro resin sponge uptake test of T3 and T4 in animals and man. Am. J. vet. Res.,30, 1471-1473.

Rabinowitz, J.L., Banks, W.C. and Greenberg, C.M. 1964. Confirmation of a new, rapid, reliable test of thyroid function of dogs. Am. J. vet. Res.,25, 1314-1316.

Rabinowitz, J.L., Shapiro, B. and Johnson, P. 1963. 'Sephadex chromatographic' test in the evaluation of thyroid function. J. nucl. Med. 4, 139-142.

Rajan, A. and Mohiyudeen, S. 1973. Blood serum cholesterol level in hypothyroidism in dogs. Kerala J. vet. Sci.,4, 117-119.

Reap, M., Cass, C. and Hightower, D. 1978. Thyroxine and triiodothyronine levels in ten species of animals. SWest. Vet.,31, 31-34.

Reed, J.H. and Femino, J. 1963. Case report. Primary hypothyroidism. Can. vet. J., 4, 26-28.

Refetoff, S., Robin,N.I.and Fang, V.S. 1970. Parameters of thyroid function in serum of 16 selected vertebrate species: A study of PBI, serum T4, free T4, and the pattern of T4 and T3 binding to serum proteins. Endocrinology, 86, 793-805.

Reid, C.F. 1968. Hypothyriodism.In Kirk, R.W. (ed.). Current Veterinary Therapy. III: Small Animal Practice. W.B. Saunders Co., Philadelphia. pp. 555-556.

Reid, C.F. 1969. Thyroid function tests in the dog. J. Am. vet. med. Ass., 155, 1571-1580.

Riggs, D.S. and Man, E.B. 1940. A permanganate acid ashing micro-method for iodine determinations. I. Values in blood of normal subjects. J. biol. Chem., 134, 193-211.

Rijnberk, A. 1971. Iodine Metabolism and Thyroid Disease in the Dog. Fellowship thesis, University of Utrecht.

Rijnberk, A. 1974. Hypothyroidism.In Kirk, R.W. (ed.). Current Veterinary Therapy V: Small Animal Practice W.B. Saunders, Philadelphia. 791-797.

Rijnberk, A. and Van der Horst, C.J.G. 1969. Investigations on iodine metabolism of normal and goitrous dogs. Zentbl. vet. med.,16a, 495-508.

Rogers, W.A., Donovan, E.F. and Kociba, G.J. 1975. Lipids and lipoproteins in normal dogs and in dogs with secondary hyperlipoproteinemia. J. Am. vet. med. Ass., 166, 1092-1100.

Rojko, J.L., Hoover, E.A. and Martin, S.L. 1978. Histologic interpretation of cutaneous biopsies from dogs with dermatologic disorders. Vet. Path., 15, 579-589.

Rosenman, R.H., Byers, S.B. and Friedman, M. 1952. The mechanism responsible for the altered blood cholesterol content in deranged thyroid states. J. Clin. Endocr. Metab., 12, 1287-1299.

Schalm, O.W., 1965. Veterinary Haematology, 2nd Ed. Lea and Febiger, Philadelphia.

Schalm, O.W. 1975. Veterinary Haematology, 3rd Ed. Lea and Febiger, Philadelphia.

Schalm, O.W., Jain, N.C. and Carroll, E.J. 1975. Veterinary Haematology. Lea and Febiger, Philadelphia. pp.

Scherzinger, E. and Grosser, I. 1973. Methods for the direct determination of the thyroid hormones content of blood. Zentbl. VetMed (1972), 19a(9), 775-786 (D, en, es, fr). Abstract 1416 Vet. Bull., 43, 162.

Schiller, I., Berglund, N.E., Terry, J.R., Reichlin, R., Trueheart, R.E. and Cox, G.E 1964. Hypercholesteremia in pet dogs. Archs. Path., 77, 389-392.

Schultz, R.D. 1974. Immunologic disorders in the dog and cat. Symposium on Allergy. Veterinary Clinics of North America, 4, 153-174.

Schwartzman, R.M. 1966. How to recognise and manage canine skin diseases of endocrine origin. Mod. Vet. Practice, 47, 47-52.

Scriba, P.C., Bauer, M., Emmert, D., Fateh-Moghadam, A., Hoffman, G.G., Horn, K. and Pickardt, C.R. 1979. Effects of obesity, total fasting and re-alimentation on L-thyroxine (T4) 3, 5, 3-L triiodothyronine (T3) 3, 3, 5-L-triiodothyronine (rT3), thyroxine binding globulin (TBG), cortisol, thyrotrophin, cortisol binding globulin (CBG), transferrin, α_2-haptoglobin and complement C3 in serum. Acta Endocr. 91, 629-643.

Shapiro, B. and Rabinowitz, J.L. 1962. Chromatographic method utilizing sephadex for the separation of free iodide, protein bound and unbound triiodothyronine in sera. .A. Clinical correlation with the Hamolsky T-3-RBC uptake method. J. nucl. Med., 3, 417-421.

Shull, K.H., Mann, G.V., Andrus, S.B. and Stare, F.J. 1954. Response of dogs to cholesterol feeding. Am. J. Physiol., 176, 475-482.

Siegel, E.T. 1971. Endocrinology. Scientific Presentation and Seminar Synopses of 38th Ann. Meeting, Am. Anim. Hosp. Ass., pp. 132-142.

Siegel, E.T. 1977. The thyroid gland .In Siegel, E.T. (ed.). Endocrine Diseases of the Dog. Lea and Febiger, Philadelphia. pp. 54-80.

Siegel, E.T. and Belshaw, B.E., 1968. Laboratory evaluation of adreno-cortical and thyroid functions in the dog . In Kirk, R.W. (ed.). Current Veterinary Therapy III: Small Animal Practice. W.B. Saunders, Philadelphia. pp. 545-551.

Sims, M.H., Redding, R.W. and Nachreiner, R.F. 1977. Depressed thyroid function in two tetraplegic dogs. J. Am. vet. med. Ass., 171, 178-80.

Singh, H.P., Hebert, M.A. and Gault, M.H. 1972. Effect of some drugs on clinical laboratory values as determined by the technicon SMA 12/60. Clin. Chem., 18, 137-143.

Smith, H.A., Jones, T.C., and Hunt, R.D. 1972. The thyroid. Veterinary Pathology, 4th Ed. pp. 1357-1358.

Smith, H.A. and Jones, T.C. 1957. Veterinary Pathology. Lea and Febiger, Philadelphia, pp. 861-866.

Sodikoff, C. 1979. Microdot T4 testing. Mod. vet. Pract., 60, 1042-1043.

Solomon, D.H., Benotti, J., De Groot, L.J., Greer, M.A., Pileggi, V.J., Pittman, J.A., Robbins, J., Selenkow, H.A., Sterling, K. and Volpe, R. 1972. A nomenclature for tests of thyroid hormones in serum: Report of a Committee of the American Thyroid Association. J. clin. Endocr. Metab., 34, 884-890.

Stein, R.B. and Price, L. 1972. Evaluation of adjusted total thyroxine (Free Thyroxine Index) as a measure of thyroid function. J. clin. Endocr. Metab., 34, 225-228.

Steiner, A. and Domanski, B. 1941. Dietary hypercholesterolemia. Am. J. med. Sci., 201, 820-830.

Steiner, A. and Kendall, F.E. 1946. Atherosclerosis and arteriosclerosis in dogs following ingestion of cholesterol and thiouracil. Archs. Path., 42, 433-444.

Sterling, K. 1968. Cited as personal communication by Furth et al., 1968.

Sterling, K. and Tabachnick, M. 1961. Resin uptake of ^{131}I- triodothyronine as a test of thyroid function. J. clin. Endocr., Metab. 21, 456-464.

Swenson, M.J. 1977. Duke's Physiology of Domestic Animals. 9th Ed. Comstock Pub. Associates, a division of Cornell University Press, Ithaca and London.

Tepperman, J. 1962. Metabolic and Endocrine Physiology. 1st Ed. Year Book Medical Publisher Inc., Chicago.

Theran, P. and Thornton, G.W. 1966. Case records of the Angell Memorial Animal Hospital. J. Am. vet. med. Ass., 148, 562-568.

Snedecor, G.W. and Irvine, M.R. 1933. On the clinical square test for homogenicity, Ames Iowa St. Coll. Sa., 8, 75-81.

Thomsett, L.R. 1966. Symposium on allergic and endocrine dermatoses in the dog and cat Part III. Endocrine disorders and hair loss in the dog. J. small Anim. Pract., 7, 777-780.

Thomsett, L.R. 1975. Some Observations on Alopecia of the Dog. F.R.C.V.S. Fellowship Thesis, London.

Thompson, K.W. and Long, C.N.H. 1941. The effect of hypophysectomy upon hypercholesterolemia of dogs. Endrocrinology, 28, 715-722.

Thomson, R.A.E. and Michaelson, S.M. 1967. A source of false iodine ^{131}uptake and protein bound iodine values in dogs. Am. J. vet. Res., 28, 1623-1625.

Tiecken, C.W. 1956. An Investication into the Function of the Thyroid Gland of the Dog. Thesis, Utrecht. Cited by Kral, F. and Schwartzman, R.M. 1964.

Trevorrow, V. 1939. Studies on the nature of the iodine in blood. J. biol. Chem., 127, 737-750.

Tucker, W.E. 1962. Thyroiditis in a group of laboratory dogs: a study of 167 beagles. Am. J. clin. Path., 38, 70-74.

Varley, H. 1967. Practical Clinical Biochemistry. William Heinemann Medical Books Ltd. London and New York. pp. 669-671.

Visconti, J. 1970. Drugs and the measurement of thyroid function. D.V.M. News Magazine pp. 10-11.

Walton, G.S. 1965. Abnormal hair growth in domestic animals .In Rook, A.J. and Walton, G.S. (eds.). Comparative Physiology and Pathology of the Skin. Blackwell Scientific Publications. pp. 211-221.

Walton K.W., Campbell, D.A., and Tonks, E.L. 1965. The significance of alterations in serum lipids in thyroid dysfunction. 1. The relation between serum lipoproteins, carotenoids and vitamin A in hypothyroidism and thyrotoxicosis. Clin.Sci. 29, 199-215

Wayne, E.J. 1960. Clinical and metabolic studies in thyroid diseases. Brit.Med.J., 1, 1-11 and 78-90.

Wilson, R.B., Dickson, W.M. and Frost, F.N. 1961. A procedure for assay of thyroid status in animals. Vet.Med., 56, 285-289.

Wolfler, A. 1879. Die Aortendruse and der Aortenkropf. Eine vorlaufige Mittheiling. Wien. med. Wschr., 5, 198. Cited by Rijnberk, A. 1971.

Wright, R.C. and Hoover, R.D. 1961. Thyroprotein for skin and hair conditions of dogs. Mod.vet.Pract., 42, (Apt. 15), (No. 8) 54-55.

Zak, B., Willard, H.H., Myers, G.B. and Boyle, A.J. 1952. Chloric acid method for determination of protein bound iodine. Anal.Chem., 24, 1345.

Zimmer, F.E. and Collins, J.A. 1967. In Conn, H.F., Chohecy, R.J. and Conn, R.B. Jun. (eds.). Current Diagnosis. W.B. Saunders, Philadelphia, pp. 432-435. Cited by Bush, B.M. (1969a).